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=> fil wpix
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=> d all abeq tech tot l34

L34  ANSWER 1 OF 2  WPIX (C) 2002 THOMSON DERWENT
AN   2000-514888 [46]   WPIX
DNC  C2000-153638
TI   Novel cell composition having antiinfectious and hematopoietic
     properties useful for restoring hematopoiesis in an aplasic
     patients, comprises macrophages, myeloid cells and
     progenitor cells.
DC   B04
IN   BARTHOLEYNS, J; KLEIN, B; LU, Z Y
PA   (IDMI-N) IDM IMMUNO-DESIGNED MOLECULES; (UYMO-N) UNIV MONTPELLIER CENT
     HOSPITALIER
CYC  89
PI   WO 2000045827 A1 20000810 (200046)* EN   24p    A61K035-28
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
            OA PT SD SE SL SZ TZ UG ZW
         W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI
            GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT
            LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ
            TM TR TT TZ UA UG US UZ VN YU ZW
     AU 2000022938 A  20000825 (200059)              A61K035-28
     EP 1150694    A1 20011107 (200168)  EN          A61K035-28
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI
ADT  WO 2000045827 A1 WO 2000-EP647 20000127; AU 2000022938 A AU 2000-22938
     20000127; EP 1150694 A1 EP 2000-901600 20000127, WO 2000-EP647 20000127
FDT  AU 2000022938 A Based on WO 200045827; EP 1150694 A1 Based on WO 200045827
PRAI EP 1999-400239   19990203
IC   ICM  A61K035-28
     ICS  A61K035-14
AB   WO 200045827 A UPAB: 20000921
     NOVELTY - A cell composition (I) comprising macrophages (Ia),
     myeloid cells (Ib) and progenitor cells (Ic), is new.
          DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
     following:
          (1) a cell composition comprising (Ia), presenting anti-infectious
     and hematopoietic properties;
          (2) preparation of (I);
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(3) a cell composition obtained by the method in (2); and

(4) a pharmaceutical composition (PC) comprising (I) as an active substance.

ACTIVITY - Cytostatic; **hematopoietic**; immunosuppressive.

MECHANISM OF ACTION - Myeloma cell growth inhibitor. Malignant cells were cultured in RPMI1640 culture medium supplemented with 10% FCS and 3 ng/ml of interleukin-6. 5 multiply 105 myeloma cells were cultured alone or with 5 multiply 105 activated MAK for 3 days. In one culture group 5 multiply 105 MAK was cultured alone. At day 1, 2 and 3 of cultures, the number of viable cells was determined using trypan blue exclusion. Addition of MAK blocked the growth of the 3 myeloma cells.

USE - (I) is useful for the preparation of drugs, for the restoration of **hematopoiesis** in an aplasic patient and/or the protection of patients against infectious diseases or against residual tumors (claimed). (I) is also useful in cancer immunotherapy and in **stem cell** transplantation.

ADVANTAGE - Expansion of **progenitor** and **stem cells** from peripheral blood without costly purification of a defined cell population is allowed under improved standardized procedures. (I) has gained a new combination of activities such as purge by **macrophages** and cytotoxic T/NK cells of the tumor cell eventually presenting in the graft, eradication of residual cancer disease by **macrophages** and/or antigen presenting cells present in the autologous or in the allogeneic grafts, avoiding most infectious episodes after injection at the beginning of aplasia period, facilitating engraftment and decreasing the aplasia period significantly by markedly increasing the recovery rate of different blood populations.

DESCRIPTION OF DRAWING(S) - The figure represents the inhibition of the growth of myeloma cell lines of the activated MAK. The number of viable cells (x104/ml) is plotted against the time (days).

Dwg.1/5

FS CPI

FA AB; GI; DCN

MC CPI: B04-F04; B04-H02; B04-H05C; B04-H06; B04-H07; B12-M07; B14-F11; B14-G02; B14-H01B

TECH UPTX: 20000921

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) is prepared by mobilizing (Ic) in the blood of a patient, for instance by premedication with G-CSF and/or GM-CSF, or G-CSF and cyclophosphamide, and thus increasing the amount of (Ic) in peripheral blood. After washing of the platelets, granulocytes and erythrocytes, blood **mononuclear** cells and (Ic) are cocultured in a medium allowing differentiation of **monocytes** into **macrophages** and **myeloid progenitors** into **polynuclear** cells for about 4-10 days. Coculture is carried out in the presence of cytokines or growth factors such as IL3, IL6, **stem cell** factor, EPO, thrombopoietin, GM-CSF, G-CSF, Flat-3 ligand, C-kit ligand or their agonist. At the end of coculture, **macrophage** is activated by adding gamma-interferon or muramyl peptides. The cells are concentrated, resuspended in a vehicle suitable for administration to the patient and a part or whole of the suspension is then subjected to freezing (claimed). Preferred Composition: (I) comprises (Ic) at a ratio of at least about 0.1% - 20%, (Ib) at an amount of 10 - 30% and (Ia) at an amount of about 10 - 60% (being expressed with respect to the total number of cells). (I) further comprises T **lymphocytes** preferably at a ratio of 10 - 60% expressed with respect to the total number of cells. (Ic) which are generated from and possibly included in peripheral blood **mononuclear** cells are **myelo**-erythroid **progenitor** cells, **myeloid progenitor** cells, lymphoid **progenitor** cells or their mixtures, further contain 0.1 - 20% of **CD34+ stem cells**. **Macrophages**, **myeloid** cells and **lymphocytes** are included in/or generated from blood **mononuclear** cells. (I) is derived from

and/or included in peripheral blood **mononuclear** cell composition comprising 10-50% of **monocytes**, 10 - 70% of **lymphocytes**, 0.1 - 20% of (Ic), 1 - 50% of **polynuclear** cells and 0.1 - 20% of **stem cells**.

L34 ANSWER 2 OF 2 WPIX (C) 2002 THOMSON DERWENT
AN **2000-259135** [23] WPIX
CR 1991-119233 [17]; 1995-346090 [45]; 2001-256683 [23]; 2001-281051 [29]; 2001-298941 [25]; 2001-353108 [25]; 2001-366062 [25]; 2001-407312 [42]; 2002-350789 [19]
DNC **C2000-079421**
TI Production of **hematopoietic** cells suitable for administration to a subject using **progenitor** cells and expanding the cells using **stem cell** factor.
DC B04 D16
IN BOSSELMANN, R A; MARTIN, F H; SUGGS, S V; ZSEBO, K M
PA (AMGE-N) AMGEN INC
CYC 14
PI EP 992579 A1 20000412 (200023)* EN 123p C12N005-06
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
ADT EP 992579 A1 Div ex EP 1990-310899 19901004, EP 1999-122861 19901004
FDT EP 992579 A1 Div ex EP 423980
PRAI US 1990-589701 19901001; US 1989-422383 19891016; US 1990-537198 19900611; US 1990-573616 19900824; WO 1990-US5548 19900928
IC ICM C12N005-06
ICS A61K035-14; A61K035-28
AB EP 992579 A UPAB: 20020618
NOVELTY - A method of making **hematopoietic** cells suitable for administration to a subject is new and comprises:
(a) obtaining **hematopoietic progenitor** cells from a donor; and
(b) expanding the cells by adding to the cells a **hematopoietically** effective dose of a polypeptide product having at least part of the primary structural confirmation and one or more of the biological properties of naturally occurring **stem cell** factor (SCF).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a method of making **hematopoietic** cells suitable for administration to a subject to effect **hematopoietic** recovery in the subject comprising:
(a) obtaining **hematopoietic progenitor** cells from a donor; and
(b) expanding the cells obtained in (a) by adding the cells a **hematopoietically** effective dose of a polypeptide product having at least part of the primary structural confirmation and one or more of the biological properties of naturally occurring **stem cell** factor (SCF);
(2) a method for making **hematopoietic** cells suitable for administration to a subject to treat **hematopoietic** disorders in the subject comprising:
(a) obtaining **hematopoietic progenitor** cells from a donor; and
(b) expanding the cells obtained in (a) by adding the cells a **hematopoietically** effective dose of a polypeptide product having at least part of the primary structural confirmation and one or more of the biological properties of naturally occurring **stem cell** factor (SCF); and
(3) a method for expanding **hematopoietic** cells ex vivo comprising:
(a) obtaining **hematopoietic progenitor** cells from a donor; and
(b) expanding the cells obtained in (a) by adding the cells a

hematopoietically effective dose of a polypeptide product having at least part of the primary structural confirmation and one or more of the biological properties of naturally occurring **stem cell** factor (SCF).

USE - The method is useful for stimulating primitive **progenitor** cells including early **hematopoietic progenitor** cells which are capable of maturing to erythroid, megakaryocyte, granulocyte, lymphocyte and **macrophage** cells. SCF results in absolute increases in **hematopoietic** cells of both **myeloid** and lymphoid lineages. SCF is useful for treating a **hematopoietic** disorder, e.g. bone marrow failure, induced by an infectious disease, HIV Induced Acquired Immunodeficiency Syndrome (AIDS), Kala Azar, miliary tuberculosis, fulminating septicemia, disseminated fungal disease, malaria (claimed), aplastic anemia, paroxysomal nocturnal hemaglobinuria, myelofibrosis, myelosclerosis, osteopetrosis, metastatic carcinoma, acute leukemia, multiple myeloma, Hodgkin's disease, sarcoidosis, primary splenic pancytopenia, vitamin B12 and folic acid deficiency, pyridoxine deficiency, Diamond Blackfan anemia, hypopigmentation disorders such as piebaldism and vitiligo. The method is useful for expanding early **hematopoietic progenitors** in syngenic, allogenic or autologous bone marrow transplant. SCF is useful for enhancing the efficiency of gene therapy based on transfecting **hematopoietic stem cells**. SCF is also useful for combating the myelosuppressive effects of anti-HIV drugs such as AZT and for enhancing **hematopoietic** recovery after acute blood loss and as a boost to the immune system for fighting neoplasia (cancer).

ADVANTAGE - The method is capable of stimulating early **progenitor** cells.

Dwg.0/47

FS CPI

FA AB; DCN

MC CPI: B04-F04; B04-H02; B04-H04; B04-H16; B14-A01; B14-A02B1; B14-A04; B14-F03; B14-G01; B14-H01; B14-N01; B14-S03; D05-H08

TECH UPTX: 20000516

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The **hematopoietic** factors had been administered to the subject prior to obtaining the cells of (a) and are obtained from the bone marrow, peripheral blood or cord blood. The **hematopoietic** cells are selected from dendritic cells, B-lymphocytes, T lymphocytes, basophils, eosinophils, neutrophils, **macrophage**, platelets, promyelocytes, metamyelocytes, myelocytes, **myeloids**, myleoblast and erythrocytes. The **hematopoietic** disorder is bone marrow failure, induced by an infectious disease, HIV Induced Acquired Immunodeficiency Syndrome (AIDS), Kala Azar, miliary tuberculosis, fulminating septicemia, disseminated fungal disease and malaria. The SCF polypeptide is selected from amino acids 1-162, 1-164 and 1-165 optionally consisting of N-terminal methionine. The SCF polypeptide is selected from amino acids 1-100, 1-110, 1-120, 1-123, 1-127, 1-130, 1-133, 1-137. 1-141, 1-145, 1-148, 1-152, 1-156, 1-157, 1-158, 1-159, 1-160, 1-161, 1-163, 1-166, 1-168, 1-173, 1-178, 2-164, 2-165, 5-164, 11-164, 1-180, 1-183, 1-185, 1-189, 1-220 and 1-248 (all amino acid sequences are fully defined in the specification) and the polypeptides optionally consist of an N-terminal methionine. The **hematopoietic progenitor** cells are exposed to **stem cell** factor in the presence of at least one other cytokine (e.g. IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, EPO, G-CSF, GM-CSF, CSF-1, IGF-1, MGDF and L1F. The **hematopoietic progenitor** cells are exposed to **stem cell** factor in the presence of at least one other **hematopoietic** factor.

TECHNOLOGY FOCUS - POLYMERS - Preferred Method: The SCF is covalently conjugated to a polymer (especially polyethylene glycol).

=> d all abeq tech tot l33

L33 ANSWER 1 OF 10 WPIX (C) 2002 THOMSON DERWENT
AN 2001-202976 [20] WPIX
DNN N2001-144806 DNC C2001-060352
TI New humanized biomaterial for use in preparing tissue implants, comprises porous biocompatible composite material implanted with **monocyte** derived cells and **macrophages**.
DC B04 D16 D21 D22 P34
IN **BARTHOLEYNS, J**
PA (IDMI-N) IDM IMMUNO-DESIGNED MOLECULES
CYC 94
PI WO 2001015753 A1 20010308 (200120)* EN 11p A61L027-40
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000072786 A 20010326 (200137) A61L027-40
ADT WO 2001015753 A1 WO 2000-EP8157 20000822; AU 2000072786 A AU 2000-72786 20000822
FDT AU 2000072786 A Based on WO 200115753
PRAI EP 1999-402149 19990830
IC ICM A61L027-40
ICS A61L027-38
AB WO 200115753 A UPAB: 20010410
NOVELTY - Humanized biomaterial (I) comprising a porous biocompatible composite material customized and implanted with **monocyte** derived cells and **macrophages**, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) living body-supporting implant (II) which comprises or consists of humanized biomaterial, and is preferably structured under the form of a scaffold, tissue-supporting sponges, bone or cartilage
(2) a process for the preparation of (I); and
(3) a process for the preparation of (II).
USE - (I) and (II) can be used for the preparation of a tissue implant (graft) destined to replace or repair defective tissue, such as defective bone, cartilage, dental tissue, fibrous tissue and fibrocartilaginous supporting tissue. The **monocyte** derived cells or **macrophages** implanted in (I) and (II) are autologous with respect to the tissue to be replaced or repaired, enabling the biomaterial or the living body-supporting implant to be recognized as self. (I) or (II) can also be implanted in a tissue, for the in vitro, in vivo or ex vivo delivery of factors chosen in the group of chemokines and/or monokines, and/or cytokines and/or growth factors, the factors released being useful for the local attraction of cells required for tissue growth (such as osteoblasts, chondrocytes, fibroblasts and epithelial cells) and/or for the neovascularization around the implanted biomaterial, and/or the growth of new tissue (claimed).
ADVANTAGE - Homogenous humanized bioactive material comprising a porous biocompatible composite material customized and implanted with **monocyte** derived cells and preferably with **macrophages**, can be used for implantation purposes and does not present the long term biocompatibility problems of prior art materials. The bioactive biomaterial enables tissue growth (for example bone and cartilage) in its porous space and secures the integration of the grafted biomaterial in the surrounding tissues. The new biomaterial also provides long lasting prostheses, which avoids requirement for replacement of biomaterial prostheses after 10 years, as often need up to now.
Dwg.0/0

FS CPI GMPI
FA AB; DCN
MC CPI: B04-E01; B04-F01; B04-F04; B04-N04; B12-M05; D05-H10; D05-H12; D08-A; D09-C01; D09-C01C; D09-C01D
TECH UPTX: 20010410

TECHNOLOGY FOCUS - BIOLOGY - Preferred Humanized Biomaterial: The biocompatible composite material is selected from microfibers, ceramic materials, metal oxides such as aluminum oxide, calcium phosphate ceramic, glass or carbon fibers, hydroxylapatite, silicon carbide or nitride and collagen polymers or a mixture of these materials. The human **macrophages** are liable to be obtained by ex vivo differentiation from blood **monocytes** leading to living **macrophages** and are cultured under conditions enabling their penetration and adherence into the biomaterial, for instance for several hours at 37 degrees Celsius, with the porous biomaterial, allowing infiltration of the biomaterial and substantially irreversible binding of the living **macrophages** to the biomaterial, being humanized with patient's **macrophages** and ready for implantation.

Preferred Implant: (II) comprises or consists of (I) and is preferably structured under the form of scaffold, tissue-supporting sponges, bone or cartilage.

Preparation: Preparation of (I) comprises the following steps:
(1) preparation of the porous biomaterial structured in the form of bones or cartilage;
(2) preparation of **macrophages** from blood **monocytes**;
(3) immersion of the biomaterial in a physiologic solution appropriate for the culture of **macrophages** which are added afterwards (phosphate buffered saline and medium such as IMDM (iscovbe's modified dulbecco's medium), AIMV and RPMI);
(4) addition of the **macrophages** to the solution under conditions enabling binding to biomaterial for 1-20 hours at 37 degrees Celsius, 5% CO2 and 5% air;
(5) washing of the biomaterial and conservation until use in physiologic medium.

Preparation of (II) comprises:
(1) preparation of a customized porous implant or scaffold composed of biocompatible material;
(2) preparation of **macrophages** from blood **monocytes** of the patient needing the customized implant of biomaterial;
(3) co-culture of **macrophages** and the implant in adequate medium under conditions enabling penetration and adherence to the biomaterial at 37 degrees Celsius, 5% CO2 in hydrophobic bags or containers until grafting the implant.

L33 ANSWER 2 OF 10 WPIX (C) 2002 THOMSON DERWENT
AN 2001-168701 [17] WPIX
DNC C2001-050426
TI Producing irreversibly differentiated dendritic cells from **mononuclear** cells, useful in immunotherapy of e.g. cancer, by culturing in presence of specific growth factors.
DC B04 D16
IN **KLEIN, B**; TARTE, K
PA (CELL-N) CELLGEN SARL; (UYMO-N) UNIV MONTPELLIER CENT HOSPITALIER; (UYHO-N) UNIV CENT HOSPITALIER
CYC 95
PI WO 2001009288 A1 20010208 (200117)* FR 43p C12N005-06
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
FR 2796961 A1 20010202 (200117) C12N005-02

AU 2000070096 A 20010219 (200129) C12N005-06
EP 1198558 A1 20020424 (200235) FR C12N005-06
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2001009288 A1 WO 2000-FR2173 20000728; FR 2796961 A1 FR 1999-9836 19990729; AU 2000070096 A AU 2000-70096 20000728; EP 1198558 A1 EP 2000-958640 20000728, WO 2000-FR2173 20000728
FDT AU 2000070096 A Based on WO 200109288; EP 1198558 A1 Based on WO 200109288
PRAI FR 1999-9836 19990729
IC ICM C12N005-02; C12N005-06
ICS A61K035-14; A61P037-00; C12N005-08
AB WO 200109288 A UPAB: 20010328
NOVELTY - Production of dendritic cells (DC) comprises growing **mononuclear** cells produced by cytopheresis after mobilization for 4-6 days, adding tumor necrosis factor alpha (TNF alpha), and optionally an inflammatory mediator, to the culture, and continuing culture for 1-4 days then recovering the DC.

DETAILED DESCRIPTION - Production of dendritic cells (DC) comprises:

(i) growing **mononuclear** cells produced by cytopheresis after mobilization for 4-6 days;

(ii) adding tumor necrosis factor alpha (TNF alpha), and optionally an inflammatory mediator, to the culture, and continuing culture for 1-4 days; then

(iii) recovering DC.

Step (i) is in serum-free medium supplemented with human albumin (HA) and in the presence of granulocyte-**macrophage** colony-stimulating factor (GM-CSF) and an interleukin (IL) that blocks differentiation into the **macrophage** lineage.

INDEPENDENT CLAIMS are also included for the following:

(1) irreversible DC that are alpha v beta 3-, alpha v beta 5+, CCR5- and CCR7+; and

(2) immunotherapeutic method that involves reinjection of autologous DC, produced by the method, then activated by specific antigens (Ag).

ACTIVITY - Cytostatic; antiviral; antiparasitic; immunostimulant.

MECHANISM OF ACTION - None given.

USE - DC are used, after activation with specific antigens, for immunotherapy of cancer and viral/parasitic infections.

DC efficiently present antigen to T **lymphocytes** and may be activated with specific antigens in vitro, reducing presentation of xenogeneic, allogenic or unidentified autologous proteins and thus non-specific immune responses. They capture tumor antigens in vivo, either by endocytosis of proteins or by phagocytosis of apoptotic cells; migrate selectively to lymph nodes (for antigen presentation) and express IL-12 which promotes differentiation of naive CD8+ cells into type 1 cytotoxic T **lymphocytes**.

ADVANTAGE - The method provides the large number of mature, irreversibly differentiated DC required for immunotherapy, e.g. a 5 hour cytophoresis will provide enough cells for 6 vaccinations, each of 109 DC. The phenotype of DC is stable after withdrawal of the cytokines present in the in vitro cultures.

Dwg.0/6
FS CPI
FA AB; DCN
MC CPI: B04-F02; B04-H02D; B04-H02P; B04-H04C; B04-H08; B04-N02; B14-A02; B14-B02; B14-G01; B14-H01; D05-H08
TECH UPTX: 20010328
TECHNOLOGY FOCUS - BIOLOGY - Preferred Process: Step (i) is for 5 days and step (ii) for 2 days. After step (i) the DC are immature, after step (ii) they are mature. The **mononuclear** cells are obtained after mobilization with chemotherapeutic agents and/or by using at least one cellular growth factor. The concentrations of GM-CSF, IL and TNF alpha are all 1-1000 ng/ml, particularly 100 ng/ml for GM-CSF and 25 ng/ml for IL, and the amount of HA is 1-2, particularly 2, wt.vol.%

In method (2), the recovered **mononuclear** cells may be frozen then thawed before culture, and activated DC may also be frozen before being reinjected.
Preferred Materials: In step (i), IL-4 or IL-13 is used to block differentiation and in step (ii) TNF alpha serves as inflammatory mediator, optionally in combination with prostaglandin E2 (at 20-1000 ng/ml).

L33 ANSWER 3 OF 10 WPIX (C) 2002 THOMSON DERWENT
AN 2001-168271 [17] WPIX
DNC C2001-050143
TI Molecular complex which binds with high affinity to **monocyte** -derived cells, includes a tissue extract and a molecular vector and is used to stimulate immune responses e.g. against tumors.
DC B04 D16
IN **BARTHOLEYNS, J**; ROMET-LEMONNE, J
PA (IDMI-N) IDM IMMUNO-DESIGNED MOLECULES
CYC 92
PI WO 2000076527 A2 20001221 (200117)* EN 14p A61K035-12
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZW
AU 2000055301 A 20010102 (200121) A61K035-12
EP 1181025 A2 20020227 (200222) EN A61K035-12
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000076527 A2 WO 2000-EP5202 20000606; AU 2000055301 A AU 2000-55301 20000606; EP 1181025 A2 EP 2000-940329 20000606, WO 2000-EP5202 20000606
FDT AU 2000055301 A Based on WO 200076527; EP 1181025 A2 Based on WO 200076527
PRAI EP 1999-401385 19990609
IC ICM A61K035-12
ICS A61K035-74; A61K035-76; A61K039-00; A61P031-00; A61P035-00; A61P043-00; C12N005-06; C12N005-08
AB WO 200076527 A UPAB: 20010328
NOVELTY - Molecular complex comprising a tissue extract containing at least one known component and unknown components, and a molecular vector, comprising a particle bearing sugars and/or polypeptides, is new. The vector is able to recognize the known component of the tissue extract, and a phagocytic receptor of **monocyte**-derived cells (MDCs). The polypeptides are not antibodies.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) MDCs prepared by contacting them with the novel molecular complex;
(2) an ex vivo method for stimulating cellular and/or humoral immune responses against unknown components of a tumor tissue extract, comprising contacting MDCs with the novel molecular complex, in which the tissue extract is a tumor tissue extract, under conditions which enable:
(a) phagocytosis of the molecular complex by MDCs;
(b) intracellular degradation and processing of the known and unknown components of the tumor tissue extract; and
(c) presentation of the known and unknown components on the peripheral membrane of the MDCs together with major histocompatibility peptide (MHC) I and II molecules;
(3) inducing in vivo specific cellular and/or humoral immune responses against unknown components of tumor tissue extract, comprising injecting the novel molecular complex;
(4) conditioning ex vivo human MDCs to acquire tissue specificity, comprising contacting MDCs with the novel molecular complex, under conditions which enable phagocytes of the molecular complex by the MDCs;

and

(5) treating diseases, by accumulating conditioned MDCs prepared by the process of (4), in specific tissue to induce tissue repair and/or regeneration, the method comprises:

(a) simultaneous and/or sequential injections of MDCs and the novel molecular complex, under conditions which enable phagocytosis; or

(b) injection of MDCs which have previously phagocytosed the novel molecular complex.

ACTIVITY - Immunomodulatory; cytostatic; antiviral; antibacterial.

USE - The molecular complex is useful for ex vivo and in vivo stimulation of cellular and/or humoral immune responses, e.g. for treatment of tumors or infections.

ADVANTAGE - The complexes have high affinity with both tissue extracts and with MDCs, and are capable of stimulating immune responses against unknown components of a tumor tissue extract.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B04-B04H; B04-C02; B04-N04; B14-A01; B14-A02; B14-H01; B14-H01B; D05-H08

TECH UPTX: 20010328

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Complex: At least one of the polypeptides or sugars in the vector recognizes the known surface component of the tissue extract, especially a known epitope such as a tumor antigen. At least one of the polypeptides or sugars, especially a mannosylated residue, recognizes phagocytic receptors of MDCs, such as receptors for mannose, oligosaccharides or Fe receptors of MDCs. The particle is a biocompatible polymer particle of size 0.1-2 micro-m. The surface polypeptides or sugars are covalently linked to the particle. The tissue extract comprises macroscopic fragments of killed, irradiated or haptenized tumor cells (e.g. lysates or apoptotic bodies), or killed pathogens (e.g. viruses or bacteria). The MDCs recognized by the molecular complex are **macrophages**, dendritic cells or antigen-presenting cells.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Extract: The tissue extract comprises normal tissue parts such as tissue membranes, tissue factors, tissue proteins, macroscopic fragments of tissue such as lysate or apoptotic bodies. The tissue originates from the thymus, lung, pancreas, cartilage, endothelium, neuromuscular junctions, prostate, sexual organs, bladder, muscles, peripheral nerves, central nervous system extracts, spleen, liver, bone, heart, or skin cells.

L33 ANSWER 4 OF 10 WPIX (C) 2002 THOMSON DERWENT

AN 2000-160368 [14] WPIX

CR 1994-200266 [24]; 1994-200267 [24]; 1995-283608 [37]; 1995-283735 [37]; 1995-283774 [37]

DNC C2000-049991

TI Treating **hematopoietic** disorders with fusion proteins comprising mutated interleukin-3 fused with secondary colony stimulating factors or other interleukin-3 variants.

DC B04 D16

IN ABRAMS, M A; BAUER, S C; BRAFORD-GOLDBERG, S R; CAPARON, M H; EASTON, A M; **KLEIN, B K**; MCKEARN, J P; OLINS, P O; PAIK, K; THOMAS, J W

PA (SEAR) SEARLE & CO G D

CYC 1

PI US 6022535 A 20000208 (200014)* 142p A61K038-20

ADT US 6022535 A CIP of US 1994-192325 19940204, Div ex WO 1995-US1185 19950202, CIP of US 1995-411795 19950406, US 1995-469318 19950606

FDT US 6022535 A CIP of US 5604116

PRAI US 1995-469318 19950606; US 1994-192325 19940204; WO 1995-US1185 19950202; US 1995-411795 19950406

IC ICM A61K038-20

ICS C07K014-54; C12N015-62
AB US 6022535 A UPAB: 20000725
NOVELTY - Methods for treating **hematopoietic** disorders with fusion proteins comprising recombinant, mutated human interleukin-3 (hIL-3) variants or mutant proteins (muteins) fused with secondary colony stimulating factors (CSFs) (e.g. cytokines, lymphokines, interleukin and/or **hematopoietic** colony stimulating factors) or other interleukin-3 variants with or without a linker, are new.

DETAILED DESCRIPTION - A method (X) of treating a patient suffering from a **hematopoietic** disorder, comprising administering a fusion protein (I) comprising recombinant, mutated human interleukin-3 (hIL-3) variants or mutant proteins (muteins) fused with secondary colony stimulating factors (CSFs) (e.g. cytokines, lymphokines, interleukins and/or **hematopoietic** colony stimulating factors) or other interleukin-3 variants with or without a linker. (I) may comprise the peptide sequences (Ia) to (Ip):

R1-L-R2 (Ia)
R2-L-R1 (Ib)
R1-R2 (Ic)
R2-R1 (Id)
Met-Ala-R1-L-R2 (Ie)
Met-Ala-R2-L-R1 (If)
Met-Ala-R1-R2 (Ig)
Met-Ala-R2-R1 (Ih)
Met-R1-L-R2 (Ii)
Met-R2-L-R1 (Ij)
Met-R1-R2 (Ik)
Met-R2-R1 (Il)
Ala-R1-L-R2 (Im)
Ala-R2-L-R1 (In)
Ala-R1-R2 (Io)
Ala-R2-R1 (Ip)

R1 = a modified hIL-3 amino acid sequence which differs from the sequence of native hIL-3 (amino acids 1 - 133) by the replacement of 4 - 44 of the residues corresponding to positions 17 - 118 of the native sequence with other amino acids;

R2 = either a colony stimulating factor, a cytokine, a lymphokine, an interleukin and/or a **hematopoietic** factor; and

L = a linker capable of linking R1 to R2.

In R1:

(1) the residues corresponding to positions 101 and 116 are not Ala or Val (respectively);

(2) no more than one of the amino acids at positions 63, 82, 87, 98 and 112 are different from the corresponding amino acids in native hIL-3;

(3) the modified sequence optionally differs from the sequence of native hIL-3 by the deletion of 1 - 14 residues from the N-terminus and/or the deletion of 1 - 15 amino acid residues from the C-terminus of native hIL-3; and

(4) has increased activity relative to native hIL-3 in at least one assay (either an AML cell proliferation assay, a TF-1 cell proliferation assay and/or a methylcellulose assay.

USE - The method (X) may be used in vivo to treat **hematopoietic** disorders resulting from bacterial, viral and fungal infections, cancer radiation therapy, chemotherapy or bone marrow suppressive drugs (claimed). It may also be used in vitro to stimulate bone marrow and blood cell activation and growth prior to infusion of the bone marrow and blood transplants into patients.

Colony stimulating factors (CSFs) which stimulate the differentiation and/or proliferation of bone marrow cells have generated much interest because of their therapeutic potential for restoring depressed levels of **hematopoietic stem cell**-derived cells. CSFs in both human and murine systems have been identified and distinguished according to their activities. For example, granulocyte-CSF (G-CSF) and

macrophage-CSF (M-CSF) stimulate the in vitro formation of neutrophilic granulocyte and **macrophage** colonies (respectively) while GM-CSF and interleukin-3 (IL-3) have broader activities and stimulate the formation of both **macrophages** and neutrophilic and eosinophilic granulocyte colonies. IL-3 also stimulates the formation of mast, megakaryocyte and pure and mixed erythroid colonies.

Because of its ability to stimulate the proliferation of a number of different cell types and to support the growth and proliferation of **progenitor** cells. IL-3 has potential for therapeutic use in restoring **hematopoietic** cells to normal amounts in those cases where the number of cells has been reduced due to diseases or to therapeutic treatments such as radiation and/or chemotherapy.

IL-3 is a hematopoietic growth factor which has the property of being able to promote the survival, growth and differentiation of hematopoietic cells. Among the biological properties of IL-3 are the ability:

(1) to support the growth and differentiation of progenitor cells committed to all, or virtually all, blood cell lineage's;

(2) to interact with early multipotential stem cells;

(3) to sustain the growth of pluripotent precursor cells;

(4) to stimulate proliferation of chronic myelogenous leukemia (CML) cells;

(5) to stimulate proliferation of mast cells, eosinophils and basophils;

(6) to stimulate DNA synthesis by human acute myelogenous leukemia (AML) cells;

(7) to prime cells for production of leukotrienes and histamines;

(8) to induce leucocyte chemotaxis; and

(9) to induce cell surface molecules needed for leukocyte adhesion.

ADVANTAGE - The fusion molecules are characterized by possessing the usual activity of both of their constituent peptides and further by having a biological or physiological activity greater than the additive function of the IL-3 or second CSF alone (i.e. the peptides act synergistically). Their activity may also be further enhanced by the mutations they comprise. The variations may further reduce undesirable side effects associated with IL-3.

Dwg.0/7

FS CPI
FA AB; DCN
MC CPI: B04-C01; B04-E02B; B04-F02; B04-F04; B04-H02C0E; B04-H0400E; B04-N03A0E; B11-C08E1; B11-C09; B14-G01; B14-G03; D05-H08; D05-H12B2; D05-H12C; D05-H17B2; D05-H17C
TECH UPTX: 20000320

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In (X), the fusion protein used may have one of a large number of amino acid sequences given in the specification.

L33 ANSWER 5 OF 10 WPIX (C) 2002 THOMSON DERWENT
AN 2000-022942 [02] WPIX
DNC C2000-005511
TI Composition for the treatment of cancer or infectious disease.
DC B04 B05 D16
IN **BARTHOLEYNS, J**; FOURON, Y; ROMET-LEMONNE, J
PA (IDMI-N) IDM IMMUNO-DESIGNED MOLECULES
CYC 87
PI WO 9951248 A1 19991014 (200002)* EN 26p A61K035-14
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9931479 A 19991025 (200011) A61K035-14
EP 1067944 A1 20010117 (200105) EN A61K035-14

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002510639 W 20020409 (200227) 27p A61K035-14
ADT WO 9951248 A1 WO 1999-EP2105 19990329; AU 9931479 A AU 1999-31479 19990329; EP 1067944 A1 EP 1999-913310 19990329, WO 1999-EP2105 19990329; JP 2002510639 W WO 1999-EP2105 19990329, JP 2000-542019 19990329
FDT AU 9931479 A Based on WO 9951248; EP 1067944 A1 Based on WO 9951248; JP 2002510639 W Based on WO 9951248
PRAI EP 1998-400783 19980402
IC ICM A61K035-14
ICS A61K045-00; A61P031-00; A61P035-00; C12N005-00; C12N005-08
ICI A61K031:00, A61K035:14, A61K038:19, A61K039:00; A61K031:00, A61K035-14; A61K035-14, A61K038:19; A61K035-14, A61K039:00
AB WO 9951248 A UPAB: 20000112
NOVELTY - Combined composition contains the following individual components, in the form of a kit-of-parts:
(a) **monocyte** derived cells, particularly cytotoxic **macrophages**; and
(b) chemotherapy or immunotherapy drugs, for the simultaneous, separate or sequential use, for the treatment of cancer or infectious diseases.
USE - The composition is useful for the treatment of cancer or infectious diseases.
Dwg.0/2
FS CPI
FA AB; DCN
MC CPI: B02-A; B02-C; B02-P; B04-A07A; B04-F04; B04-H02B; B04-H02N; B04-H04; B04-H05C; B04-M01; B05-A03B; B10-A07; B10-A13D; B14-H01; D05-H07; D05-H08
TECH UPTX: 20000112
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred materials: The **monocyte** derived cells contain chemotherapy or immunotherapy drugs. The chemotherapy drug is selected among cytotoxic compounds such as anthracyclins, daunorubicin, adriamycin, taxoter derivatives, vinca alkaloids, vincristine, taxol, carmustine, cisplatin, fluorouracils, cytostatic compounds such as polyamine inhibitors, topoisomerase inhibitors, tamoxifen, prodasone, or sandostatin, or compounds inducing apoptosis such as sodium butyrate or mitomycin C, antibiotics such as penicillins, P-lactamines, cephalosporins, cyclins, aminoglucosides, macrolides or sulfamides, or antiviral drugs such as AZT, protease inhibitors or acyclovir, retrovir or foscarnet. The immunotherapy drug is selected from cytokines such as cyclosporin, azathioprine, cyclophosphamide, IFN-gamma, IL-12, IL-2, GM-CSF, G-CSF, immuno-adjuvants such as murapeptides or BCG, and vaccines directed against tumor or infectious antigens, in the presence or not of adjuvants.
Preparation: The **monocyte** derived cells are such as prepared by:
(i) recovery of blood derived **mononuclear** cells directly from blood apheresis or from blood bag collection, followed if necessary by centrifugation, to eliminate a substantial part of red blood cells granulocytes and platelets, and collection of peripheral blood leukocytes;
(ii) washing peripheral blood leukocytes by centrifugation (to remove 90% of platelets, red blood cells and debris) to obtain **mononuclear** cells;
(iii) resuspension of the total **mononuclear** cells (**monocytes** + **lymphocytes**) obtained at the preceding step in culture medium (RPMI or IMDM type) at 106 to 2.107 cells/ml, possibly completed by cytokines and/or autologous serum, and culture for 5-10 days at 37 degreesC under O2/CO2 atmosphere in hydrophobic gas permeable bags, to obtain **monocyte** derived cells and contaminating **lymphocytes**.
The process comprises the additional step of freezing at temperature below or equal to -80 degreesC aliquots of the above said suspension, with the addition of a cryo-preservative. The process comprises the additional step of melting said above frozen aliquots at a temperature enabling to obtain

a suspension of **monocyte** derived cells, for instance at 4 degreesC, washing said suspension and resuspending it, for instance in an isotonic medium, to obtain a suspension of **monocyte** derived cells.

L33 ANSWER 6 OF 10 WPIX (C) 2002 THOMSON DERWENT
AN 1999-610844 [52] WPIX
DNC C1999-177800
TI Derived cells used in pharmaceuticals to stimulate wound healing.
DC A96 B04 D16
IN **BARTHOLEYNS, J**; CHOKRI, M; LATOUR, N
PA (IDMI-N) IDM IMMUNO-DESIGNED MOLECULES
CYC 87
PI WO 9950391 A1 19991007 (199952)* EN 38p C12N005-06
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9936013 A 19991018 (200010)
EP 1066370 A1 20010110 (200103) EN C12N005-06
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002509715 W 20020402 (200225) 41p C12N015-09
ADT WO 9950391 A1 WO 1999-EP2106 19990329; AU 9936013 A AU 1999-36013 19990329; EP 1066370 A1 EP 1999-917889 19990329, WO 1999-EP2106 19990329; JP 2002509715 W WO 1999-EP2106 19990329, JP 2000-541279 19990329
FDT AU 9936013 A Based on WO 9950391; EP 1066370 A1 Based on WO 9950391; JP 2002509715 W Based on WO 9950391
PRAI EP 1998-400742 19980330
IC ICM C12N005-06; C12N015-09
ICS A61K035-14; A61K039-00; A61P035-00; C12N005-10
AB WO 9950391 A UPAB: 19991210
NOVELTY - Stimulated **monocyte** derived cells (I) are new.

DETAILED DESCRIPTION - (I) present the following characteristics: (a) increased release, with respect to normal **monocyte** derived cells, of at least one of the following polypeptides, proteins or compounds: platelet derived growth factor (PGDF), insulin growth factor IGF1), **macrophage** derived growth factor (MDGF), basic fibroblast growth factor (bFGF), granulocyte **macrophage** - colony stimulating factor (GM-CSF), heat shock or stress proteins, chemokines and monokines such as interleukin (IL)-1 alpha and interferon (IFN)- gamma enzymes or enzyme inhibitors, complement components, transfer proteins, peroxides, nitrous oxide (NO), bioactive lipids, hormones, and increased presence, on their membranes, with respect to normal **monocyte** derived cells, of at least one of the following activation markers : CD1 alpha , CD11a, CD80, CD83, CD86, major histocompatibility complex (MHC) class I and MHC class II molecules, adhesins, or accessory molecules for imunostimulation such as ICAM, or CD40; and/or (b) presence in their nucleus of at least one exogenous nucleic acid which has been integrated in the absence of the **monocyte** derived cell division.

INDEPENDENT CLAIMS are also included for the following:

(1) a process for the preparation of (I), comprising stimulating of the **monocyte** derived cells by physical means such as: thermal stress (heating at 40-50oC for at least 30 minutes), pressure change (from 1-0,05 bar, or from 1-10 bars), microwaves, electric shock (about 1-10 s at about 250 mV), or electropulsation;

(2) a process for the preparation of (I), comprising: (a) preparation of **monocyte** derived cells according to the following method: (i) recovery of blood derived **mononuclear** cells directly from blood apheresis or from blood bag collection, followed if necessary by centrifugation, to eliminate a substantial part of red blood cells granulocytes and platelets, and collection of peripheral blood leukocytes;

(ii) washing peripheral blood leukocytes obtained at the preceding steps for instance by centrifugation (to remove 90% of platelets, red blood cells and debris) to obtain **mononuclear** cells; (iii) resuspension of the cells (**monocytes** + **lymphocytes**) obtained at the preceding step in culture medium (AIM-V, RPMI or IMDM type) at 106-2.107 cells/ml, possibly completed by cytokines and/or autologous serum, and culture for 5-10 days at 37 oC under O2/CO2 atmosphere in hydrophobic gas permeable bags, to obtain **monocyte** derived cells and contaminating **lymphocytes**; and (b) stimulation of the **monocyte** derived cells as described in (1);

(3) cells obtained by (1) and (2);

(4) pharmaceutical composition comprising (I) in association with a vehicle; (4) use of (I) for the preparation of a medicament for the treatment of tissue; and

(5) use of (I) for the preparation of a vaccine against tumors or infectious agents, or of a medicament for treating polypeptide or protein deficiency in a patient.

ACTIVITY - Vulnery; cytostatic.

MECHANISM OF ACTION - Vaccine.

USE - (I) is used to prepare a medicament for the treatment of wounds or polypeptide or protein deficiency, and to prepare vaccines against tumors or infectious agents (claimed).

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: A12-V01; B04-F04; B11-B; B14-H01; B14-N17B; D05-H08; D05-H13
TECH UPTX: 19991210

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred cells: The activation markers are present at at least 1000 molecules/cell. The polypeptides, proteins or compounds are released in an amount higher than 1 pg/cell/hr and the activation markers are present in the range of 103-105 molecules/cell. Preferred methods: The preparation of (I) further comprise the additional step of centrifugation of (I) at a temperature enabling cell preservation, for instance at 4 degreesC, and resuspension, for instance in isotonic medium containing autologous serum. The processes also comprise the addition of a cryopreservative such as polyethyleneglycol, glycerol, DMSO. Preferred pharmaceuticals: The pharmaceutical composition is in the form of sterile injectable preparations or of sterile topical preparations; or in the form of a vaccine comprising, as active substance (I), having integrated in their nucleus an exogenous nucleic acid coding for a polypeptide or protein which is immunogenic with respect to pathogens involved in the pathology to be treated.

L33 ANSWER 7 OF 10 WPIX (C) 2002 THOMSON DERWENT
AN 1999-347126 [29] WPIX
DNN N1999-259569 DNC C1999-102069
TI Diagnosis and treatment of pathologies.
DC B04 D16 S03
IN **BARTHOLEYNS, J**; CHOKRI, M; DREYFUS, P A; GARCIA, L; PARRISH, E; PELTEKIAN, E
PA (IDMI-N) IDM IMMUNO-DESIGNED MOLECULES; (INRM) INSERM INST NAT SANTE & RECH MEDICALE
CYC 83
PI WO 9913054 A2 19990318 (199929)* EN 24p C12N005-08
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9894410 A 19990329 (199932) C12N005-08
EP 1009806 A2 20000621 (200033) EN C12N005-08
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

JP 2001515713 W 20010925 (200170) 34p C12N005-06
ADT WO 9913054 A2 WO 1998-EP5707 19980831; AU 9894410 A AU 1998-94410 19980831; EP 1009806 A2 EP 1998-947533 19980831, WO 1998-EP5707 19980831; JP 2001515713 W WO 1998-EP5707 19980831, JP 2000-510843 19980831
FDT AU 9894410 A Based on WO 9913054; EP 1009806 A2 Based on WO 9913054; JP 2001515713 W Based on WO 9913054
PRAI US 1997-924830 19970905
IC ICM C12N005-06; C12N005-08
ICS A61K035-14; A61K038-00; A61K038-18; A61K048-00; A61P009-10; A61P011-00; A61P019-02; A61P019-08; A61P021-00; A61P025-00; A61P025-02; C12N005-10; C12N015-09; G01N033-50; G01N035-14
AB WO 9913054 A UPAB: 19990723
NOVELTY - Diagnosis and treatment of pathologies comprises administration of exogenous **monocyte** derived cells loaded with corrective agents or a marker for detection is new.

DETAILED DESCRIPTION - Treatment or diagnosis of pathologies either expressed in injured or pathological multiple sites in tissues or in the body or expressed in injured or pathological sites of tissues or cells in sites of the body, which are difficult to access, with the sites or areas in immediate proximity to the sites being the source of the release of chemotactic factors for endogenous **macrophages**, either spontaneously or upon suitable stimulation, where the treatment is carried out by administration to the body of an appropriate amount of exogenous **monocyte** derived cells (MDCs). The MDCs are, in the case of treatment, loaded with corrective agents with respect to the pathologies to be treated. The MDCs also have the properties of mobilization towards the source of the released chemotactic factors and to target the cells present in the vicinity of the released chemotactic factors. In the case of diagnosis, the MDC's are loaded with a marker enabling the detection of injured or pathological sites.

INDEPENDENT CLAIMS are also included for the following:

(1) MDCs obtained by culturing blood **mononuclear** cells to obtain **monocytes** derived cargo cells, containing a therapeutic agent for a given pathology corresponding to loaded chemical or biological substances such as peptides, polypeptides, proteins and nucleic acids or virus or nucleic acids which have been transfected into the cells or these cells loaded externally on the membrane with emitting signals. The cells have one or more of the following properties:

(i) their preparation specifically induce an increased membrane expression level of chemotactic receptors;

(ii) they are sensitive, particularly in vivo, to chemotactic factors released by sites of call or suffering cells;

(iii) they have membrane plasticity such that they can enter difficult injured sites to access such as the central nervous system (CNS);

(iv) they can rapidly reach sites of call, as soon as 2 hours to 3 days, particularly 2 to 3 days after systemic injection;

(v) they can accumulate into injured sites of call;

(vi) they remain alive in the vicinity of the injured or pathological sites for several months, particularly at least up to about 4 months;

(vii) their morphology becomes similar to the morphology of the cells normally present in the injured sites or pathological sites and they integrate the tissue cells of the injured or pathological sites; and

(viii) they can release the contained corrective agent in the sites of call, either constitutively or on demand by induction of secretion of the corrective agent;

(2) a kit for the preparation of MDCs as in (1) comprising:

(a) a culture device (bags and reagents) for the maturation of **mononuclear** cells into phagocytes, particularly **macrophages**;

(b) therapeutic agents to be introduced into the phagocytes and a device for introducing them to obtain MDCs.

USE - The method can be used for the treatment of pathologies

particularly having multiple expressed sites resulting from disseminated cancers or from inflammatory diseases (claimed). Pathologies which may be treated by the method include:

(1) for the central nervous system (CNS): genetic diseases (e.g. adrenoleukodystrophy, spinal muscular atrophy, Gauchers disease and Huntingtons disease), and sporadic diseases (e.g. Alzheimers disease, Parikinsons disease, amyotrophic lateral sclerosis, multiple sclerosis, strokes, glioblastoma, cerebral metastasis, infection of the CNS); and

(2) for the peripheral nervous and muscular system: genetic diseases (e.g. Duchenne disease, Becker's disease, muscular dystrophies), non genetic diseases (e.g. neuropathies and muscular necrosis from different origins including trauma), rheumatoid arthritis, atheromatosis, bone trauma or bone infection or degenerescence and pulmonary fibrosis (claimed).

Dwg.0/4

FS CPI EPI
FA AB; DCN
MC CPI: B04-F04; B14-C09B; B14-J01; B14-K01; B14-N01; D05-H08; D05-H09; D05-H13; D05-H14B2
EPI: S03-E14H
TECH UPTX: 19990723

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Kit: The kit may contain at least one of the following components:
(i) means for viral transduction of the phagocytes with defective viral vectors to obtain **monocyte** derived cells;
(ii) description of physical (laser, puncture, irradiation) and chemical means to induce the local signal when required, including the time schedule;
(iii) reagents for the quality control of the viral transduction and of MDC's;
(iv) software for the standard operating procedures and traceability of:
(a) phagocyte culture;
(b) introduction of corrective agents;
(c) viral transduction, and
(d) the recovery of the MDC's.

L33 ANSWER 8 OF 10 WPIX (C) 2002 THOMSON DERWENT
AN 1998-001784 [01] WPIX
DNC C1998-000705
TI Isolated **macrophage** derived antigen presenting cells - obtained using histamine agonist, H.
DC B04 D16
IN **BARTHOLEYNS, J**; CHOKRI, M; ROMET-LEMONNE, J; ROMET-LEMONNE; ROMETLEMONNE, J
PA (IDMI-N) IDM; (IDMI-N) IDM IMMUNO-DESIGNED MOLECULES
CYC 77
PI EP 808897 A1 19971126 (199801)* EN 18p C12N005-08
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
WO 9744441 A1 19971127 (199802) EN 29p
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU
AU 9729615 A 19971209 (199824) C12N005-08
EP 925356 A1 19990630 (199930) EN C12N005-08
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2000503545 W 20000328 (200026) 48p C12N015-09
AU 732536 B 20010426 (200128) C12N005-08
ADT EP 808897 A1 EP 1996-401099 19960521; WO 9744441 A1 WO 1997-EP2703 19970515; AU 9729615 A AU 1997-29615 19970515; EP 925356 A1 EP 1997-924012 19970515, WO 1997-EP2703 19970515; JP 2000503545 W JP 1997-541583 19970515, WO 1997-EP2703 19970515; AU 732536 B AU 1997-29615 19970515

FDT AU 9729615 A Based on WO 9744441; EP 925356 A1 Based on WO 9744441; JP 2000503545 W Based on WO 9744441; AU 732536 B Previous Publ. AU 9729615, Based on WO 9744441
PRAI EP 1996-401099 19960521
IC ICM C12N005-08; C12N015-09
ICS A61K031-4164; A61K031-417; A61K035-14; A61K038-00; A61K039-00; A61K039-02; A61K045-00; A61P037-04; C07K014-705; C07K016-46; C12N005-10; C12P021-02; G01N033-53
AB EP 808897 A UPAB: 19980107
Macrophages (A) have the following properties:
(a) they present on their surface:
(i) antigen CD14 with a mean intensity of 20-200;
(ii) antigen CD64 with a mean intensity of 20-200;
(b) they are devoid of the surface antigens CD1a and CD1c, the presence and mean intensities respectively of CD14, CD64 and the absence of CD1a and CD1c being for instance determined by immuno-fluorescence staining and flow cytometry analysis;
(c) they present a phagocytosis property such as determined by the following test: the phagocytosis capacity being evaluated by an uptake of formalin fixed yeast, e.g. by culturing **macrophages** for 2 hours, adding yeast in 1/10 **macrophages**/yeast ratio and incubating at 37 deg. C, 5% CO2 atmosphere for 2-3 hours, fixing by the May-Grunwald-Giemsa (MGG) staining, and the percentage of phagocytic **macrophages** being quantified for instance by microscopic analysis;
(d) they have the property of stimulating the proliferation of allogenic **lymphocytes** such as determined by the following test: allogenic primary mixed **lymphocytes** reaction (MLR) was carried out in 96-well microtitre plates by adding different numbers (2 multiply 103 to 2 multiply 105 in 100 mu l medium/well) of **macrophages** to 2 multiply 105 in 100 mu l medium/well of allogenic T cells purified from buffy coats and after 5 days incubation at 37 deg. C, cell proliferation was assessed by a colorimetric method, such as the hydrolysis of tetrazolium salt WST-1 (slightly red) to Formozan (dark red).
Also claimed are:
(1) a cell processor or kit containing:
(a) a device for the recovery of **lymphocytes** and **monocytes** free of contaminants;
(b) appropriate buffer and wash solutions and possibly an appropriate device for the conservation of **macrophages**;
(c) a device for preparing a culture for the **monocytes** and possibly the **lymphocytes** and containing histamine, cimetidine or a H2 antagonist in combination or not with GM-CSF; (d) possibly a device for transfection of cultured cells and a device for targeting antigens to **macrophages**;
(2) bispecific antibodies liable to recognise an antigen of a **macrophage** as in (A) and an antigen of a tumoral cell or of a pathogen which is to be targeted to the **macrophage**, and
(3) the use of an agonist of histamine, in particular histamine, and a H2 antagonist, in particular cimetidine, in combination or not with GM-CSF, for the preparation of **macrophages** having properties as in (A).
USE - The **macrophages** show high phagocytosis and can provide very potent antigen presenting cells. They can be directed against antigens of tumour cells or pathogens for therapeutic treatment.
Dwg.0/1
FS CPI
FA AB
MC CPI: B04-F02; B04-F04; B04-G01; B07-D09; B14-A01; B14-H01; D05-H08

L33 ANSWER 9 OF 10 WPIX (C) 2002 THOMSON DERWENT
AN 1995-006773 [01] WPIX
DNC C1995-002426
TI New **macrophage**(s) with increased cytotoxicity - useful for

treatment of cancer and as drug carriers.
DC B04 B07 D16
IN **BARTHOLEYNS**, J; CHOKRI, M
PA (IDMI-N) IDM IMMUNO-DESIGNED MOLECULES
CYC 4
PI WO 9426875 A1 19941124 (199501)* EN 25p C12N005-08
W: AU CA JP US
AU 9480504 A 19941212 (199521) C12N005-08
JP 08510118 W 19961029 (199705) 31p C12N005-06
US 5662899 A 19970902 (199741) 9p C12N005-08
AU 701147 B 19990121 (199915)# C12N005-08
US 6001351 A 19991214 (200005) A61K048-00
US 6051432 A 20000418 (200026) C12Q001-00
ADT WO 9426875 A1 WO 1993-EP1232 19930518; AU 9480504 A WO 1993-EP1232 19930518, AU 1994-80504 19930518; JP 08510118 W WO 1993-EP1232 19930518, JP 1994-524843 19930518; US 5662899 A WO 1993-EP1232 19930518, US 1995-374629 19950117; AU 701147 B AU 1994-80504 19930518; US 6001351 A Div ex WO 1993-EP1232 19930518, Div ex US 1995-374629 19950117, US 1997-896498 19970718; US 6051432 A Div ex WO 1993-EP1232 19930518, Div ex US 1995-374629 19950117, Div ex US 1997-896498 19970718, Div ex US 1999-304563 19990504, US 1999-400875 19990922
FDT AU 9480504 A Based on WO 9426875; JP 08510118 W Based on WO 9426875; US 5662899 A Based on WO 9426875; AU 701147 B Previous Publ. AU 9480504, Based on WO 9426875
PRAI WO 1993-EP1232 19930518; AU 1994-80504 19930518
REP 09Jnl.Ref
IC ICM A61K048-00; C12N005-06; C12N005-08; C12Q001-00
ICS A61K035-14; A61K035-26; A61K035-28; C12N015-85; C12P021-08; G01N033-53
AB WO 9426875 A UPAB: 19950110
Macrophages which have 1 of the following properties is new: (1) their cytotoxic activity without IFN-gamma is increased by about 20-30% w.r.t. standard **macrophages** and is pref. about 70%; (2) their cytotoxic activity with IFN-gamma is increased by about 20-40% w.r.t. standard **macrophages** and is pref. about 93%; and (3) the extension of the deactivation of the cytotoxic activity in reply to an activation of IFN-gamma is in a ratio such that, after 50 hrs. of activation with IFN-gamma, the cytotoxic activity is 30 (pref. about 55)%, compared to the max. cytotoxic activity represented by the **macrophages** due to IFN-gamma activation. The cytotoxic activity is measured as the % of inhibition of 3-H thymidine incorporation by target tumoral cells, partic. U937 cells. Also claimed is a kit comprising: means for the recovery of **lymphocytes** and **monocytes** free of contaminants; appropriate buffer and wash solns. and possibly appropriate means for the conservation of **macrophages**; means for preparing a culture medium for the **monocytes** and possibly the **lymphocytes** and contg. 1,25-dihydroxy vitamin D3 and GM-CSF; and possibly IFN-gamma.
USE - The **macrophages** can be used for the treatment of cancer, opt. with **lymphocytes**. They may contain exogenous nucleic acids and/or drugs. Dosage is pref. 2x109 to 5x109 **macrophages**. Dosage of **lymphocytes** is 4x109 to 10x109.
Dwg.1/1
FS CPI
FA AB; GI; DCN
MC CPI: B04-F01; D05-H01
ABEQ US 5662899 A UPAB: 19971013
Macrophages have at least one of the following properties:
their cytotoxic activity without IFN- gamma is increased by about 20 to 30% with respect to standard **macrophages**;
their cytotoxic activity with IFN- gamma is increased by about 20 to about 40% with respect to standard **macrophages**;
deactivation of the cytotoxic activity following activation of IFN-

gamma is such that sixty hours after activation with IFN- gamma , the residual cytotoxic activity is at least 30% of the maximum cytotoxic activity presented by the **macrophages** due to IFN- gamma activation, with said cytotoxic activity being measured as a percentage of the inhibition of 3-H thymidine incorporation by target tumoral cells, particularly U 937 cells;

said **macrophages** being prepared by culturing healthy human **monocytes** and **lymphocytes** in a culture medium containing 1,25-dihydroxy vitamin D3 and GM-CSF.

Dwg.0/1

L33 ANSWER 10 OF 10 WPIX (C) 2002 THOMSON DERWENT
AN 1991-267129 [36] WPIX
DNC C1991-115837
TI Prodn. of **macrophage**(s), growth factors, etc. - by incubating **monocytes** or leukocytes in medium contg. amino acid, glucose and vitamin(s).
DC B04 D16
IN **BARTHOLEYN, J**
PA (NATR-N) FONDATION NAT TRANS
CYC 14
PI WO 9112316 A 19910822 (199136)*
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: US
FR 2657783 A 19910809 (199144)
ADT FR 2657783 A FR 1990-1402 19900207
PRAI FR 1990-1402 19900207
REP 1.Jnl.Ref; EP 205387; FR 2624742
IC A61K035-14; A61K045-05; C12N005-00
AB WO 9112316 A UPAB: 19930928
The following are claimed: (A) a compsn. comprising differentiated **macrophages** in culture in a glycerol medium; (B) a glycosylated growth factor with a mol. wt. below 20,000 (c) a process for preparing blood cell derivs. by treating **monocytes** or leukocytes in a medium contg. at least 1g/l amino acid(s) at least 3 g/l glucose and at least 10 mg/l vitamins in a gas-permeable bag.

USE - The process may be used to obtain differentiated **macrophages**, growth factors, monokines and protease inhibitors. The **macrophages** may be used in tumour therapy, to combat infections or to promote debridement and cicatrisation of wounds. The growth factors may be used to promote wound cicatrisation, in cosmetic surgery and cosmetology, to promote neovascularisation, to combat cell ageing, to promote bone repair, in the treatment of osteoporosis, autoimmune diseases, arthritis, and ulcers, in ophthalmology and odontology, to regenerate nerves etc. @(22pp Dwg.No.0/0)
FS CPI
FA AB
MC CPI: B04-B04D1; B04-B04J; B12-A01; B12-A06; B12-A07; B12-D02A; B12-D03; B12-D09; B12-E08; B12-G01B3; B12-G04A; B12-G07; B12-J08; B12-L03; B12-L04; D05-H08; D05-H13

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FILE LAST UPDATED: 06 MAY 2002 <20020506/UP>
MOST RECENT DERWENT DPCI UPDATE 200203
PATENTS CITATION INDEX, COVERS 1973 TO DATE

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L74 ANSWER 1 OF 1 DPCI (C) 2002 THOMSON DERWENT
AN 2000-514888 [46] DPCI
DNC C2000-153638
TI Novel cell composition having antiinfectious and hematopoietic properties useful for restoring hematopoiesis in an aplasic patients, comprises macrophages, myeloid cells and progenitor cells.
DC B04
IN BARTHOLEYNS, J; KLEIN, B; LU, Z Y
PA (IDMI-N) IDM IMMUNO-DESIGNED MOLECULES; (UYMO-N) UNIV MONTPELLIER CENT HOSPITALIER
CYC 89
PI WO 2000045827 A1 20000810 (200046)* EN 24p A61K035-28
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZW
AU 2000022938 A 20000825 (200059) A61K035-28
EP 1150694 A1 20011107 (200168) EN A61K035-28
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000045827 A1 WO 2000-EP647 20000127; AU 2000022938 A AU 2000-22938 20000127; EP 1150694 A1 EP 2000-901600 20000127, WO 2000-EP647 20000127
FDT AU 2000022938 A Based on WO 200045827; EP 1150694 A1 Based on WO 200045827
PRAI **EP 1999-400239 19990203**
IC ICM A61K035-28
ICS A61K035-14
FS CPI

CTCS CITATION COUNTERS

PNC.DI	0	Cited Patents Count (by inventor)
PNC.DX	5	Cited Patents Count (by examiner)
IAC.DI	0	Cited Issuing Authority Count (by inventor)
IAC.DX	3	Cited Issuing Authority Count (by examiner)
PNC.GI	0	Citing Patents Count (by inventor)
PNC.GX	0	Citing Patents Count (by examiner)
IAC.GI	0	Citing Issuing Authority Count (by inventor)
IAC.GX	0	Citing Issuing Authority Count (by examiner)
CRC.I	0	Cited Literature References Count (by inventor)
CRC.X	0	Cited Literature References Count (by examiner)

CDP CITED PATENTS UPD: 20010424

Cited by Examiner

CITING PATENT	CAT	CITED PATENT	ACCNO
WO 200045827 A	Y	EP 241578 A	1987-293113/42
PA: (MARR-N) MARROW GRP INT; (NAUG-I) NAUGHTON B A; (ADTI-N) ADVANCED TISSUE SCI INC; (MARR-N) MARROW-TECH INC; (MARR-N) MARROW GROUP INT			
IN: NAUGHTON, G K; NAUGHTON, B A			
	Y	EP 451611 A	1991-304676/42

PA: (SYST-N) SYSTEMIX INC; (NOVS) NOVARTIS AG; (SANO) SANDOZ ERFINDUNGEN VERWALT GMBH; (SANO) SANDOZ LTD; (SANO) SANDOZ PATENT GMBH
IN: AIHARA, Y; BAUM, C M; TSUKAMOTO, A; WEISSMAN, I
Y US 5672346 A 1994-048533/06
PA: (INDV) UNIV INDIANA FOUND
IN: BRANDT, J E; HOFFMAN, R; SROUR, E F; ZANJANI, E D; SROUR, E; ZANJANI, E
Y WO 9221402 A 1992-433400/52
PA: (IMMV) IMMUNEX CORP
IN: GILLIS, S
Y WO 9716535 A 1997-272105/24
PA: (SANO) SANDOZ LTD; (SYST-N) SYSTEMIX INC; (NOVS) NOVARTIS AG; (NOVS) NOVARTIS-ERFINDUNGEN VERW GES MBH; (SANO) SANDOZ PATENT GMBH; (SANO) SANDOZ-ERFINDUNGEN VERW GMBH
IN: MURRAY, L J; YOUNG, J C

=> fil hcaplus
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FILE COVERS 1907 - 20 Jun 2002 VOL 136 ISS 25
FILE LAST UPDATED: 18 Jun 2002 (20020618/ED)

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=> d all tot l73

L73 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:202605 HCAPLUS
DN **128:275058**
TI Hematopoietic cells, **compositions** and methods
IN Taichman, Russell S.; Emerson, Stephen G.
PA Regents of the University of Michigan, USA
SO U.S., 38 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A01N063-02
ICS C12N005-00; C12N005-06
NCL 424093100
CC 63-3 (Pharmaceuticals)

Section cross-reference(s): **9**, 13

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5733541	A	19980331	US 1995-426792	19950421

AB Processes, **compns**. and uses of hematopoietic cells are disclosed. Hematopoietic cells are cells which can differentiate into mature blood cells when co-cultured with osteoblasts. Specifically, a process for propagating and maintaining the immature morphol. of a hematopoietic cell by co-culturing with osteoblasts is disclosed. The osteoblasts provide cytokines and/or a microenvironment which propagates and maintains the immature morphol. of a hematopoietic cell. Hematopoietic cells are useful in the treatment of certain blood related disorders and are useful for treatment of patients in need of hematopoietic cells.

ST hematopoietic cell culture osteoblast blood transfusion

IT Histocompatibility antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(HLA-DR, lymphocyte bearing; process for propagating and maintaining immature morphol. of hematopoietic cells by co-culturing with osteoblasts)

IT Antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(Lin, lymphocyte not bearing; process for propagating and maintaining immature morphol. of hematopoietic cells by co-culturing with osteoblasts)

IT Antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(Thy-1, lymphocyte bearing; process for propagating and maintaining immature morphol. of hematopoietic cells by co-culturing with osteoblasts)

IT Centrifugation
(equil.-d.; process for propagating and maintaining immature morphol. of hematopoietic cells by co-culturing with osteoblasts)

IT Antibodies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(hematopoietic cell-binding; process for propagating and maintaining immature morphol. of hematopoietic cells by co-culturing with osteoblasts)

IT **CD34** (antigen)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(lymphocyte bearing; process for propagating and maintaining immature morphol. of hematopoietic cells by co-culturing with osteoblasts)

IT Blood transfusion
(of hematopoietic cells; process for propagating and maintaining immature morphol. of hematopoietic cells by co-culturing with osteoblasts)

IT Animal tissue culture
Basophil
Bone marrow
Cell adhesion
Cell differentiation
Eosinophil
Erythrocyte
Hematopoietic precursor cell
Lymphocyte
Mast cell
Monocyte

Neutrophil
Osteoblast
Platelet (blood)
(process for propagating and maintaining immature morphol. of hematopoietic cells by co-culturing with osteoblasts)

IT Cytokines
Stem cell factor
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(process for propagating and maintaining immature morphol. of hematopoietic **cells** by co-culturing with osteoblasts)

IT 7440-70-2, Calcium, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(medium contg.; process for propagating and maintaining immature morphol. of hematopoietic cells by co-culturing with osteoblasts)

IT 83869-56-1, Granulocyte **macrophage** colony stimulating factor
143011-72-7, Gcsf
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(process for propagating and maintaining immature morphol. of hematopoietic cells by co-culturing with osteoblasts)

L73 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:196174 HCAPLUS
DN **126:222612**
TI Stroma-derived **stem cell** proteoglycan growth factor
IN McGlave, Philip B.; Verfaillie, Catherine M.; Gupta, Pankaj
PA Regents of the University of Minnesota, USA
SO U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 293,466, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM C12N005-00
ICS A16K038-16; C07K014-475
NCL 435377000
CC **9-11** (Biochemical Methods)
Section cross-reference(s): 15
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5605829	A	19970225	US 1994-346893	19941130
	US 5523286	A	19960604	US 1993-152051	19931112
PRAI	US 1993-152051		19931112		
	US 1994-293466		19940819		

AB This invention provides a stroma-derived anionic fraction comprising at least 1 macromol. which, in combination with cytokines, can support conservation and differentiation of long-term bone marrow culture-initiating **cells**, preferably in **stem-cell** enriched cultured hematopoietic **cells**, such as the Lin-/**CD34**+/HLA-DR- **cells** of C. Verfaillie et al. (1990). The anionic macromol.-contg. **compn**. may be isolated from stroma **cell**-conditioned media, or a compd. of substantially equiv. bioactivity may be prepd. synthetically. The bioactive anionic macromol. fraction comprises a mixt. of glycoproteins, including proteoglycans. Described is the prepn. of a synthetic proteoglycan that has a core protein and a polysaccharide portion and that can promote differentiation and maintain the self-renewal capacity of long-term bone marrow culture initiating **cells** in cultured mammalian hematopoietic **cells**, wherein the polysaccharide portion of the

synthetic proteoglycan is heparan sulfate, chondroitin sulfate, dermatan sulfate or a combination thereof and the core protein is ovalbumin.

ST stroma **stem cell** proteoglycan growth factor; bone marrow culture initiating **cell** proteoglycan; mammalian hematopoietic **cell** culture growth factor; ovalbumin glycosaminoglycan conjugate synthetic proteoglycan prepn

IT Animal **cells**
(Lin-**CD34**+DR-; stroma-derived **stem cell** proteoglycan growth factor)

IT Containers
(**cell** culture chamber; stroma-derived **stem cell** proteoglycan growth factor)

IT Ovalbumin
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(glycosaminoglycan conjugates; stroma-derived **stem cell** proteoglycan growth factor)

IT **Cell** (biological)
(**stem**; stroma-derived **stem cell** proteoglycan growth factor)

IT **Cell** differentiation
Cell proliferation
Hematopoiesis
Hematopoietic precursor cell
Mammal (Mammalia)
Microporous membranes
Tissue culture (animal)
(stroma-derived **stem cell** proteoglycan growth factor)

IT Glycosaminoglycans, biological studies
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(stroma-derived **stem cell** proteoglycan growth factor)

IT Interleukin 6
Leukemia inhibitory factor
Macrophage inflammatory protein 1.alpha.
Stem cell factor
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(stroma-derived **stem cell** proteoglycan growth factor)

IT Cytokines
RL: BAC (Biological activity or effector, except adverse); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(stroma-derived **stem cell** proteoglycan growth factor)

IT Glycoproteins (general), biological studies
RL: BAC (Biological activity or effector, except adverse); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(stroma-derived **stem cell** proteoglycan growth factor)

IT Proteoglycans, biological studies
RL: BAC (Biological activity or effector, except adverse); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(stroma-derived **stem cell** proteoglycan growth factor)

IT **CD34** (antigen)
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(stroma-derived **stem cell** proteoglycan growth factor)

IT Bone marrow

(stroma; stroma-derived **stem cell** proteoglycan growth factor)

IT Glycoproteins (specific proteins and subclasses)
RL: BAC (Biological activity or effector, except adverse); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(sulfoglycoproteins; stroma-derived **stem cell** proteoglycan growth factor)

IT 83869-56-1, GM-CSF 143011-72-7, G-CSF
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(stroma-derived **stem cell** proteoglycan growth factor)

IT 9007-28-7DP, Chondroitin sulfate, ovalbumin conjugates 9050-30-0DP, Heparan sulfate, ovalbumin conjugates 24967-94-0DP, Dermatan sulfate, ovalbumin conjugates
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(stroma-derived **stem cell** proteoglycan growth factor)

IT 1892-57-5, 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide
RL: RCT (Reactant)
(stroma-derived **stem cell** proteoglycan growth factor)

L73 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN **1996:551423** HCAPLUS
DN **125:190011**
TI Method for preparing **macrophages**, and kits and **compositions** therefor
IN Romet-Lemonne, Jean-Loup; Chokri, Mohamed
PA I.D.M. Immuno-Designed Molecules, Fr.
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA French
IC ICM A61K035-14
ICS C12N005-08
CC **9-11** (Biochemical Methods)
Section cross-reference(s): 13, 15
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9622781	A1	19960801	WO 1996-FR121	19960124
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
	FR 2729570	A1	19960726	FR 1995-785	19950124
	FR 2729570	B1	19970228		
	CA 2210449	AA	19960801	CA 1996-2210449	19960124
	AU 9646265	A1	19960814	AU 1996-46265	19960124
	AU 720285	B2	20000525		
	EP 806959	A1	19971119	EP 1996-901848	19960124
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	JP 11505512	T2	19990521	JP 1996-522679	19960124
	US 5804442	A	19980908	US 1996-654383	19960528
	US 6140122	A	20001031	US 1998-25454	19980218
	US 6221576	B1	20010424	US 1999-404643	19990923
PRAI	FR 1995-785	A	19950124		
	WO 1996-FR121	W	19960124		
	US 1996-654383	A3	19960528		

US 1998-25456 B3 19980218

AB A method is disclosed for prepg. a **compn.** contg. optionally activated **macrophages**, and/or cells derived from monocytes having a high antigen presentation potential, wherein the monocytes in the starting **compn.** are cultured, this step being preceded and/or followed by removal of at least some of the components other than monocytes from the starting **compn.**, by means of antibodies to such components, and/or followed by elutriation. **Compns.** and kits for carrying out the method are also disclosed.

ST culture **macrophage** monocyte derived cell kit; antibody cell sepn **macrophage** culture

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(MAX-1; **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Animal tissue culture
Blood platelet
Erythrocyte
Immunity
Leukocyte
Lymphocyte
Macrophage
Monocyte
(**macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Antigens
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(**macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Antibodies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(B7/BB-1, **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(B70, **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(CD3, **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(CD58, **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Immunoglobulin receptors
Receptors
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(Fc.gamma.RI (IgG fragment Fc receptor I), **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Immunoglobulin receptors

Receptors
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(Fc.gamma.RIII (IgG fragment Fc receptor III), **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Histocompatibility antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(HLA-DR, **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Glycoproteins, specific or class
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(ICAM-1 (intercellular adhesion mol. 1), **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(L-CA (leukocyte common antigen), **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Glycolipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LPS-LBP (lipopolysaccharide-contg. lipopolysaccharide-binding protein), receptors, antigen CD14-contg., **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Receptors
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(glycolipoprotein LPS-LBP, antigen CD14, **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Leukocyte
(granulocyte, **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Lymphokines and Cytokines
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(interleukin 13, **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Lymphokines and Cytokines
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(interleukin 4, **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Amino acids, biological studies
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(nonessential, **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Lymphokines and Cytokines
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(tumor necrosis factor-.alpha., **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT Interferons
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(.gamma., **macrophage** and/or monocyte-derived cell culture and **compn.** and kit)

IT 51-45-6, Histamine, biological studies 53-86-1, Indomethacin 56-85-9, L-Glutamine, biological studies 57-92-1, Streptomycin, biological studies 60-24-2, Mercaptoethanol 61-33-6, biological studies 67-97-0, Vitamin D3 127-17-3, Pyruvic acid, biological studies 39537-23-0, L-Alanyl-L-glutamine 83869-56-1, Granulocyte

macrophage colony-stimulating factor
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**macrophage** and/or monocyte-derived cell culture and **compn**. and kit)

L73 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:452344 HCAPLUS
DN **125:109686**
TI Regulation of neural **stem cell** proliferation
IN Weiss, Samuel; Reynolds, Brent A.
PA Neurospheres Holdings Ltd., Can.
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N005-06
ICS C12N005-08; A61K038-18; A61K031-20
CC **9-11** (Biochemical Methods)
Section cross-reference(s): 13, 14
FAN.CNT 8

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9615226	A1	19960523	WO 1995-CA637	19951114
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5750376	A	19980512	US 1995-483122	19950607
US 5851832	A	19981222	US 1995-486648	19950607
AU 9538367	A1	19960606	AU 1995-38367	19951114
AU 716811	B2	20000309		
EP 792350	A1	19970903	EP 1995-936393	19951114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1170435	A	19980114	CN 1995-196842	19951114
JP 10509592	T2	19980922	JP 1995-515600	19951114
FI 9701956	A	19970704	FI 1997-1956	19970507
NO 9702171	A	19970707	NO 1997-2171	19970512
PRAI US 1994-338730	A2	19941114		
US 1991-726812	B2	19910708		
US 1992-961813	B1	19921016		
US 1992-967622	B1	19921028		
US 1993-10829	B1	19930129		
US 1993-149508	YY	19931109		
US 1994-221655	B1	19940401		
US 1994-270412	B2	19940705		
US 1994-311099	YY	19940923		
US 1994-359345	A	19941220		
US 1994-359945	B2	19941220		
US 1995-376062	B2	19950120		
US 1995-385404	B2	19950207		
WO 1995-CA637	W	19951114		

AB The invention is directed to the regulation of multipotent neural **stem cell** proliferation in vitro and in vivo using **compns**. comprising various biol. factors. More particularly, the invention is related to a method and therapeutic **compns**. for regulating the no. of precursor **cells** that are produced by dividing neural **stem cells**, by exposing the **stem cells** to specific biol. factors or combinations thereof.

ST multipotent neural **stem cell** proliferation regulation; CNS neural **stem cell** proliferation regulation; spinal cord injury nerve **cell** proliferation

IT Animal tissue culture
Cell proliferation
Granulation tissue
Mammal
(regulation of multipotent neural **stem cell** proliferation)

IT Animal growth regulators
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(regulation of multipotent neural **stem cell** proliferation)

IT Neuroglia
(astroglia, regulation of multipotent neural **stem cell** proliferation)

IT Animal growth regulators
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blood platelet-derived growth factors, regulation of multipotent neural **stem cell** proliferation)

IT Animal growth regulators
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone morphogenetic proteins, regulation of multipotent neural **stem cell** proliferation)

IT Nervous system
(central, disease, injury, regulation of multipotent neural **stem cell** proliferation)

IT Animal growth regulators
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ciliary neurotrophic factors, regulation of multipotent neural **stem cell** proliferation)

IT Neuroglia
(disease, gliosis, regulation of multipotent neural **stem cell** proliferation)

IT Spinal cord
(disease, injury, regulation of multipotent neural **stem cell** proliferation)

IT Brain, disease
Nerve, disease
(injury, regulation of multipotent neural **stem cell** proliferation)

IT Lymphokines and Cytokines
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interleukin 2, regulation of multipotent neural **stem cell** proliferation)

IT Lymphokines and Cytokines
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interleukin 6, regulation of multipotent neural **stem cell** proliferation)

IT Lymphokines and Cytokines
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interleukin 8, regulation of multipotent neural **stem cell** proliferation)

IT Lymphokines and Cytokines
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**macrophage** inflammatory protein 1.alpha., regulation of multipotent neural **stem cell** proliferation)

IT Lymphokines and Cytokines
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**macrophage** inflammatory protein 1.beta., regulation of multipotent neural **stem cell** proliferation)

IT Lymphokines and Cytokines
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**macrophage** inflammatory protein 2, regulation of multipotent neural **stem cell** proliferation)

IT Nucleotides, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligo-, deoxyribo-, antisense; regulation of multipotent neural **stem cell** proliferation)

IT Neuroglia
(oligodendroglia, regulation of multipotent neural **stem cell** proliferation)

IT Lymphokines and Cytokines
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor necrosis factor-.alpha., regulation of multipotent neural **stem cell** proliferation)

IT Animal growth regulators
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.-transforming growth factors, regulation of multipotent neural **stem cell** proliferation)

IT Animal growth regulators
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-transforming growth factors, regulation of multipotent neural **stem cell** proliferation)

IT 302-79-4, Retinoic acid 9050-30-0, Heparan sulfate 9061-61-4, NGF 62229-50-9, EGF 106096-92-8, Acidic FGF 106096-93-9, Basic FGF 114949-22-3, Activin 117147-70-3, Amphiregulin 179047-85-9 179047-86-0 179047-87-1 179047-88-2 179047-89-3 179047-90-6 179047-91-7 179047-92-8
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(regulation of multipotent neural **stem cell** proliferation)

L73 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:446851 HCAPLUS
DN **125:81293**
TI Methods of obtaining **compositions** enriched for hematopoietic **stem cells, compositions** derived therefrom and methods of use thereof
IN Hill, Beth L.; Chen, Benjamin P.; Simmons, Paul J.
PA Systemix, Inc., USA; Hanson Centre for Cancer Research
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N005-08
ICS C07K016-28; A61K035-28; C12P021-08
CC **9-11** (Biochemical Methods)
Section cross-reference(s): 13
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 9615229	A1	19960523	WO 1995-IB1003	19951113
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5677136	A	19971014	US 1994-340047	19941114
	CA 2203525	AA	19960523	CA 1995-2203525	19951113
	AU 9537527	A1	19960606	AU 1995-37527	19951113
	EP 787181	A1	19970806	EP 1995-935547	19951113
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 10513341	T2	19981222	JP 1995-515883	19951113
PRAI	US 1994-340047		19941114		
	WO 1995-IB1003		19951113		

AB Methods resulting in the isolation from populations of hematopoietic **cells** of **compns**. enriched for **stem cells** are provided. The methods use an antibody specific for a unique epitope on the CD59 **cell** surface protein that is accessible to a high degree on **stem cells** (**CD34**+HCC-1+) while being less accessible or absent on more mature **cells** (**CD34**+HCC-1lo/-). Pos. selection of **stem cells** with antibodies that recognize this epitope is used in combination with selection for **cells** expressing the **CD34** marker to obtain a **cell** population enriched for **stem cells**. Neg. selection is used independently, or in conjunction with 1 or both of the above methods, in a **stem cell** enrichment scheme. The enriched population of **cells** derived from these methods is also provided and designated **CD34**+HCC-1+.

ST hematopoietic **stem cell** isolation **CD34** antibody; HCC1 antibody hematopoietic **stem cell** isolation

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(C-Kit; methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Animal **cell** line
(**CD34**+HCC-1+; methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(HCC-1; methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Animal tissue culture
Bone marrow
Cell differentiation
Hematopoiesis
Hybridoma
Leukemia
Thymus gland
(methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Transferrin receptors
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Antibodies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

(Uses)
(methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(rholo; methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Glycophorins
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(A, methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(CD19, methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(CD2, methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(CD33, methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**CD34**, methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(CD38, methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(CD59, methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Immunoglobulin receptors
Receptors
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(Fc.gamma.RIII (IgG fragment Fc receptor III), methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Histocompatibility antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(HLA-DR, methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Glycolipoproteins
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(LPS-LBP (lipopolysaccharide-contg. lipopolysaccharide-binding protein), receptors, antigen CD14-contg., methods and **compns**. for obtaining hematopoietic **stem cells**)

IT Immunoglobulins
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST

(Analytical study); PREP (Preparation); USES (Uses)
(M, FITC conjugates; methods and **compns.** for obtaining hematopoietic **stem cells**)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(SSEA-1 (stage-specific embryonic antigen 1), methods and **compns.** for obtaining hematopoietic **stem cells**)

IT Lymphocyte
(T-**cell**, methods and **compns.** for obtaining hematopoietic **stem cells**)

IT Antigens
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(Thy-1, methods and **compns.** for obtaining hematopoietic **stem cells**)

IT **Hematopoietic precursor cell**
(**erythroid** burst-forming, methods and **compns.** for obtaining hematopoietic **stem cells**)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(glycolipoprotein LPS-LBP, antigen CD14, methods and **compns.** for obtaining hematopoietic **stem cells**)

IT **Hematopoietic precursor cell**
(granulocyte-**erythroid-macrophage**-monocyte colony-forming, methods and **compns.** for obtaining hematopoietic **stem cells**)

IT **Hematopoietic precursor cell**
(granulocyte-**macrophage** colony-forming, methods and **compns.** for obtaining hematopoietic **stem cells**)

IT Antibodies
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal, methods and **compns.** for obtaining hematopoietic **stem cells**)

IT **Hematopoietic precursor cell**
(**stem**, methods and **compns.** for obtaining hematopoietic **stem cells**)

IT Receptors
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(transferrin, methods and **compns.** for obtaining hematopoietic **stem cells**)

IT 62669-70-9, Rhodamine 123
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(methods and **compns.** for obtaining hematopoietic **stem cells**)

IT 27072-45-3DP, FITC, IgM conjugates
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(methods and **compns.** for obtaining hematopoietic **stem cells**)

L73 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:212061 HCAPLUS
DN **120:212061**
TI **CD34**-positive HLA-DR-negative KR-positive Human **stem cell compositions**, isolation of these **cells**, and methods and uses
IN Srour, Edward F.; Zanjani, Esmail D.; Brandt, John E.; Hoffman, Ronald
PA Indiana University Foundation, USA

SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K035-28
ICS C12N005-02; C12N005-08
CC **9-11** (Biochemical Methods)
Section cross-reference(s): 13, 15
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9402157	A1	19940203	WO 1993-US7059	19930727
	W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	EP 658114	A1	19950621	EP 1993-918427	19930727
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

PRAI US 1992-919447 19920727
US 1993-77134 19930615
WO 1993-US7059 19930727

AB Methods are disclosed for isolating **cells** populations that are highly enriched for human pluripotent hematopoietic **stem cells**. The **cells** are **CD34**+, HLA-DR- and express the receptor for the c-kit ligand (KR+). Methods or growing the **cells** in long term bone marrow cultures in the presence of c-kit ligand and other cytokines are disclosed. The **cells** may be useful for transplantation and for use in gene therapy protocols. In utero transplantation of the **CD34**+ HLA-DR- **cells** for the establishment of chimeric sheep is also described.

ST human pluripotent hematopoietic **stem cell** isolation

IT **Hematopoietic precursor cell**
(BFU-MK, of bone marrow or peripheral blood of breast cancer patient, **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation in relation to)

IT Transplant and Transplantation
(**CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation for)

IT Erythropoiesis
(**CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation in relation to)

IT **Hematopoietic precursor cell**
(CFU-MK, of bone marrow or peripheral blood of breast cancer patient, **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation in relation to)

IT Antigens
RL: BIOL (Biological study)
(KR (c-kit ligand receptor), hematopoietic **stem cell** of human pos. for and **CD34**+/HLA-DR-, isolation of)

IT Sheep
(chimeric, **CD34**+/HLA-DR- human hematopoietic **stem cell** in establishment of)

IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(in **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation)

IT Antigens
RL: BIOL (Biological study)
(**CD34**, hematopoietic **stem cell** of human pos. for and HLA-DR-/KR+, isolation of)

IT Antigens
RL: BIOL (Biological study)
(CD71, **CD34**+/HLA-DR-/KR+ hematopoietic **stem**

cell of human neg. for, isolation of)
IT Histocompatibility antigens
RL: BIOL (Biological study)
(HLA-DR, hematopoietic **stem cell** of human neg. for and **CD34**+/KR+, isolation of)
IT Antigens
RL: BIOL (Biological study)
(SSEA-1 (stage-specific embryonic antigen 1), **CD34**+/HLA-DR-/KR+ hematopoietic **stem cell** of human neg. for, isolation of)
IT **Hematopoietic precursor cell**
(**erythroid** burst-forming, of bone marrow or peripheral blood of breast cancer patient, **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation in relation to)
IT **Hematopoietic precursor cell**
(granulocyte-**erythroid-macrophage**-monocyte colony-forming, of bone marrow or peripheral blood of breast cancer patient, **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation in relation to)
IT **Hematopoietic precursor cell**
(granulocyte-**erythroid**-monocyte-megakaryocyte colony-forming unit, of bone marrow or peripheral blood of breast cancer patient, **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation in relation to)
IT **Hematopoietic precursor cell**
(granulocyte-**macrophage** colony-forming, of bone marrow or peripheral blood of breast cancer patient, **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation in relation to)
IT Receptors
RL: BIOL (Biological study)
(hematopoietic **cell** growth factor KL, ligand for, in **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation)
IT Hemopoietins
RL: BIOL (Biological study)
(hematopoietic **cell** growth factors KL, receptors, ligand for, in **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation)
IT **Hematopoietic precursor cell**
(high-proliferation-potential colony-forming, of bone marrow or peripheral blood of breast cancer patient, **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation in relation to)
IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 3, **CD34**+/HLA-DR- human hematopoietic **stem cell** mobilization in presence of GM-CSF and)
IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 3, fusion products, with GM-CSF, in **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation)
IT Hematopoiesis
(megakaryocytopoiesis, **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation in relation to)
IT Leukocyte
(mononuclear, phenotypic anal. of, of breast cancer patient, **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation in relation to)
IT Hematopoiesis
(myelopoiesis, **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation in relation to)

IT Mammary gland
(neoplasm, mononuclear **cells** of patient with, phenotypic anal. of, **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation in relation to)
IT **Hematopoietic precursor cell**
(**stem**, isolation of, of human, **CD34**+/HLA-DR-/KR+)
IT 50-18-0, Cyclophosphamide
RL: BIOL (Biological study)
(**CD34**+/HLA-DR- human hematopoietic **stem cell** mobilization in presence of)
IT 83869-56-1, GM-CSF
RL: BIOL (Biological study)
(**CD34**+/HLA-DR- human hematopoietic **stem cell** mobilization in presence of IL-3 and)
IT 62669-70-9, Rhodamine 123
RL: BIOL (Biological study)
(**CD34**+/HLA-DR-/KR+ hematopoietic **stem cell** of human dull for, isolation of)
IT 83869-56-1D, GM-CSF, interleukin-3 fusion products
RL: BIOL (Biological study)
(in **CD34**+/HLA-DR-/KR+ human hematopoietic **stem cell** isolation)

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FILE 'WPIX' ENTERED AT 14:54:16 ON 20 JUN 2002

FILE LAST UPDATED: 18 JUN 2002 <20020618/UP>
MOST RECENT DERWENT UPDATE 200238 <200238/DW>
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=> d all abeq tech tot

L81 ANSWER 1 OF 2 WPIX (C) 2002 THOMSON DERWENT
AN 1994-048533 [06] WPIX
DNC C1994-021910
TI Human pluripotent haematopoietic stem cell compsn. for transplants and gene therapy - comprises CD34+, HLA-DR- and expresses the receptor for the C-kit ligand (KRf).
DC B04 D16
IN BRANDT, J E; HOFFMAN, R; SROUR, E F; ZANJANI, E D; SROUR, E; ZANJANI, E
PA (INDV) UNIV INDIANA FOUND
CYC 45
PI WO 9402157 A1 19940203 (199406)* EN 85p A61K035-28
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AU BB BG BR BY CA CZ FI HU JP KP KR KZ LK MG MN MW NO NZ PL RO RU

SD SK UA VN
AU 9347880 A 19940214 (199425) A61K035-28
EP 658114 A1 19950621 (199529) EN A61K035-28
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
EP 658114 A4 19960710 (199644) A61K035-28
US 5672346 A 19970930 (199745) 25p A61K035-14 <--
ADT WO 9402157 A1 WO 1993-US7059 19930727; AU 9347880 A AU 1993-47880 19930727, WO 1993-US7059 19930727; EP 658114 A1 EP 1993-918427 19930727, WO 1993-US7059 19930727; EP 658114 A4 EP 1993-918427 ; US 5672346 A CIP of US 1992-919447 19920727, US 1993-77134 19930615
FDT AU 9347880 A Based on WO 9402157; EP 658114 A1 Based on WO 9402157
PRAI US 1992-919447 19920727; US 1993-77134 19930615
REP 06Jnl.Ref; 3.Jnl.Ref
IC ICM A61K035-14; A61K035-28
ICS C12N005-02; C12N005-08
AB WO 9402157 A UPAB: 19940322
A human pluripotent haematopoietic stem cell (PHSC) contg. compsn. comprises a homogeneous popln. of human haematopoietic cells characterised as CD34+, HLA -DR-, KR+, the cells being capable of in vitro self-renewal and differentiation to members of at least the erythroid, myeloid and megakaryocytic lineages.

Also claimed are: (1) methods for recovering a PHSC-enriched cell fraction from its cellular mixt. with committed progenitors and dedicated lineages, the cell fraction having the properties above, by sepg. from the cellular mixt. a homogeneous popln. of human haematopoietic cells characterised as CD34+, HLA-DR- and KR+; and (2) a human-PHSC contg. cell popln. in a culture medium having an expanded number of cells characterised as CD34+, HLA-DR-.

Initially the cellular mixt., e.g. adult human bone marrow is treated to remove cells associated with dedicated lineages, e.g. by counterflow centrifugal elutriation, resulting in at least a 2-fold enrichment of cells for CD34+ and HLA-DR-. These cells are combined with fluorochrome-labelled antibodies to CD34, HLA-DR and KR and cells characterised as CD34+, HLA-DR-, KR+ are recovered by means of the fluorochromes.

USE - The methods provide for isolating cell poplns. that are highly enriched for human PHSC cells which are CD34+, HLA-DR- and express the receptor for the C-kit ligand (KR+). The cells may be grown in long term bone marrow cultures in the presence of the C-kit ligand and other cytokines. The cells may be useful for transplantation and for use in gene therapy protocols.

Dwg.0/6
FS CPI
FA AB
MC CPI: B04-F04; D05-H08; D05-H13
ABEQ US 5672346 A UPAB: 19971113
A method of obtaining persistent maintenance of grafted human hematopoietic cells in a mammal, comprising the step of grafting the mammal in utero with a pluripotent human stem cell (PHSC) containing population of non-fetal human hematopoietic cells characterized as CD34+ and which undergo self-renewal and differentiation to members of the lymphoid, myeloid, erythroid and megakaryocytic lineages when cultured in vitro.

Dwg.0/6

L81 ANSWER 2 OF 2 WPIX (C) 2002 THOMSON DERWENT
AN 1992-433400 [52] WPIX
DNN N1992-330747 DNC C1992-192396
TI Use of haematopoietic progenitor cells for autologous cell transplantation - expanded exo vivo with growth factor for haematopoietic rescue after cyto-reductive therapy.
DC B04 D16 P34
IN GILLIS, S

PA (IMMV) IMMUNEX CORP
CYC 19
PI WO 9221402 A1 19921210 (199252)* EN 21p A61M037-00 <--
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: AU CA JP
AU 9221793 A 19930108 (199315) A61M037-00
US 5199942 A 19930406 (199316) 9p A61M037-00
EP 587754 A1 19940323 (199412) EN A61M037-00
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
JP 06508613 W 19940929 (199443) A61K035-14
AU 665955 B 19960125 (199611) C12N005-08
EP 587754 A4 19970101 (199842) A61M037-00
ADT WO 9221402 A1 WO 1992-US4686 19920605; AU 9221793 A AU 1992-21793 19920605, WO 1992-US4686 19920605; US 5199942 A CIP of US 1991-712315 19910617, US 1991-765844 19910926; EP 587754 A1 EP 1992-913333 19920605, WO 1992-US4686 19920605; JP 06508613 W WO 1992-US4686 19920605, JP 1993-500649 19920605; AU 665955 B AU 1992-21793 19920605; EP 587754 A4 EP 1992-913333
FDT AU 9221793 A Based on WO 9221402; EP 587754 A1 Based on WO 9221402; JP 06508613 W Based on WO 9221402; AU 665955 B Previous Publ. AU 9221793, Based on WO 9221402
PRAI US 1991-712315 19910607; US 1991-765844 19910926
REP US 4778879; US 4863727; US 5004681; US 5035994; US 5078996; US 5100378; US 5106733; 1.Jnl.Ref; WO 9102754; WO 9211355; WO 9218615; WO 9318136
IC ICM A61K035-14; A61M037-00; C12N005-08
ICS A61K035-28
ICA A61K037-02
AB WO 9221402 A UPAB: 19931118
A method for autologous haematopoietic cell transplantation in a patient receiving cytoreductive therapy is claimed comprising: (a) removing haematopoietic progenitor cells from the patient prior to cytoreductive therapy; (b) expanding the haematopoietic progenitor cells ex vivo with a growth factor selected from granulocyte macrophage-colony stimulating factor (GM-CSF), steel factor (SF), interleukin-3 (IL-3) interleukin-1 (IL-1) and GM-CSF/IL-3 fusion proteins to provide a cellular prepn. comprising an expanded population of haematopoietic progenitor cells with the proviso that IL-1 is used in combination with at least one other ex vivo growth factor; and (c) administering the cellular population to the patient following cytoreductive therapy.

USE/ADVANTAGE - The ex vivo progenitor cell expansion in medium contg. the growth factor is capable of expanding myeloid and erythroid progenitor cells populations and improves the ability of the expanded population of progenitor cells to engraft and proliferate in bone marrow and other haematopoietic tissue when later administered in an autologous transplantation.

Dwg.0/0
FS CPI GMPI
FA AB
MC CPI: B04-B04A3; B04-B04A6; B04-B04D4; B04-B04J; B04-C01G; B12-G07; D05-H08
ABEQ US 5199942 A UPAB: 19931006
Autologous haematopoietic cell transplantation in a patient receiving cytoreductive therapy comprises (a) removing haematopoietic progenitor cells prior to therapy; (b) expanding the cells ex vivo with (i) a GM-CSF with IL-3 or a GM-CSF/IL-3 fusion protein, and (ii) one of more of steel factor, IL-1 and G-CSF; and (c) administering the cells to the patient following cytoreductive therapy.

USE/ADVANTAGE - Used to counteract the myelosuppressive effects of cytoreductive therapy.

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=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 14:54:29 ON 20 JUN 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 20 Jun 2002 VOL 136 ISS 25
FILE LAST UPDATED: 18 Jun 2002 (20020618/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d all tot l78

L78 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:316565 HCAPLUS
DN 130:335019
TI Three-dimensional cartilage cultures using transforming growth factor-.beta.
IN Purchio, Anthony F.; Zimber, Michael; Dunkelman, Noushin; Naughton, Gail K.; Naughton, Brian A.
PA Advanced Tissue Sciences, Inc., USA
SO U.S., 41 pp., Cont.-in-part of U.S. Ser. No. 254,096.
CODEN: USXXAM
DT Patent
LA English
IC C12N005-00; A01N001-02; A61K035-12; A61K035-32
NCL 435240230
CC 9-11 (Biochemical Methods)
Section cross-reference(s): 1, 2, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5902741	A	19990511	US 1995-463566	19950605	
	CA 1282725	A1	19910409	CA 1986-512230	19860623	
	JP 62249926	A2	19871030	JP 1986-191567	19860815	
	EP 241578	A2	19871021	EP 1986-111709	19860823	<--
	EP 241578	A3	19890726			
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
	EP 309456	A1	19890405	EP 1987-903124	19870415	
	EP 309456	B1	19950913			
	R: AT, BE, DE, FR, GB, IT, LU, NL, SE					
	HU 202578	B	19910328	HU 1987-2758	19870415	
	AU 615414	B2	19911003	AU 1987-73568	19870415	
	RO 106655	B1	19930630	RO 1987-135557	19870415	
	JP 2857392	B2	19990217	JP 1987-502719	19870415	
	CA 1310926	A1	19921201	CA 1987-534951	19870416	
	ZA 8702805	A	19871125	ZA 1987-2805	19870421	

NO	8705286	A	19871217	NO 1987-5286	19871217
NO	179181	B	19960513		
NO	179181	C	19960821		
IL	85957	A1	19940624	IL 1988-85957	19880401
US	4963489	A	19901016	US 1988-242096	19880908
US	5032508	A	19910716	US 1989-402104	19890901
IL	91536	A1	19961031	IL 1989-91536	19890906
WO	9002796	A1	19900322	WO 1989-US3853	19890907
	W: AU, BB, BG, BR, DK, FI, HU, JP, KR, LK, MC, MG, MW, NO, RO, SD, SU				
	RW: BF, BJ, CF, CG, CM, GA, ML, MR, SN, TD, TG				
AU	8942114	A1	19900402	AU 1989-42114	19890907
AU	644578	B2	19931216		
EP	358506	A3	19900523	EP 1989-309085	19890907
EP	358506	A2	19900314		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
BR	8907642	A	19910820	BR 1989-7642	19890907
HU	56393	A2	19910828	HU 1989-5973	19890907
JP	04501657	T2	19920326	JP 1989-509402	19890907
CA	1335657	A1	19950523	CA 1989-610617	19890907
JP	2000189158	A2	20000711	JP 1999-364942	19890907
JP	2001258555	A2	20010925	JP 2001-32776	19890907
ZA	8906886	A	19900627	ZA 1989-6886	19890908
US	5266480	A	19931130	US 1990-575518	19900830
AU	9068159	A1	19910314	AU 1990-68159	19901218
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NO	9100787	A	19910422	NO 1991-787	19910227
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CA	2192064	AA	19951214	CA 1995-2192064	19950606
WO	9533821	A1	19951214	WO 1995-US7296	19950606
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, UZ, VN				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU	9527696	A1	19960104	AU 1995-27696	19950606
AU	689605	B2	19980402		
EP	812351	A1	19971217	EP 1995-923009	19950606
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP	2002502226	T2	20020122	JP 1996-501308	19950606
JP	10114664	A2	19980506	JP 1997-268792	19971001
JP	3032492	B2	20000417		
US	5858721	A	19990112	US 1997-978520	19971125
US	5962325	A	19991005	US 1998-157306	19980918
US	6140039	A	20001031	US 1999-237980	19990125
US	6022743	A	20000208	US 1999-264513	19990308
AU	9947557	A1	19991202	AU 1999-47557	19990913
AU	729774	B2	20010208		
PRAI US	1986-853569	B1	19860418		
US	1987-36154	A2	19870403		

US 1987-38110 B2 19870414
US 1988-242096 A2 19880908
US 1989-402104 A3 19890901
US 1990-575518 A3 19900830
US 1993-131361 A2 19931004
US 1994-254096 A2 19940606
JP 1987-502719 A3 19870415
WO 1987-US869 W 19870415
JP 1989-509402 A3 19890907
WO 1989-US3853 A 19890907
US 1994-241259 A3 19940511
US 1995-418238 A3 19950406
US 1995-463566 A 19950605
WO 1995-US7296 W 19950606
US 1995-487749 A1 19950607
AU 1996-60315 A3 19960603
US 1999-237980 A1 19990125

AB The present invention relates to a method of stimulating the proliferation and appropriate cell maturation of a variety of different cells and tissues in three-dimensional cultures in vitro using TGF-.beta. in the culture medium. In accordance with the invention, stromal cells, including, but not limited to, chondrocytes, chondrocyte-progenitors, fibroblasts, fibroblast-like cells, umbilical cord cells or bone marrow cells from umbilical cord blood are inoculated and grown on a three-dimensional framework in the presence of TGF-.beta.. Stromal cells may also include other cells found in loose connective tissue such as endothelial cells, macrophages/monocytes, adipocytes, pericytes, reticular cells found in bone marrow stroma, etc. The stromal cells and connective tissue proteins naturally secreted by the stromal cells attach to and substantially envelope the framework composed of a biocompatible non-living material formed into a three-dimensional structure having interstitial spaces bridged by the stromal cells. The living stromal tissue so formed provides the support, growth factors, and regulatory factors necessary to sustain long-term active proliferation of cells in culture and/or cultures implanted in vivo. When grown in this three-dimensional system, the proliferating cells mature and segregate properly to form components of adult tissues analogous to counterparts in vivo. Chondrocytes were prepd. from articular cartilage of healthy mature cows or New Zealand white rabbits and seeded in polyglycolic acid mesh sterilized by ethylene oxide or electron beam treatment. Chondrocytes grown in the three-dimensional matrix in the presence of TGF-.beta.1 produced cartilage tissue which was smoother, more glistening and had a more solid consistency than the tissue grown in cultures without TGF-.beta.1. Addn. of ascorbate had a stimulating effect which was additive with TGF-.beta..

ST cartilage culture transforming growth factor beta; three dimensional stromal cell tissue culture; chondrocyte culture polyglycolate mesh TGF beta

IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(CMP (cartilage matrix protein), nutrient medium contg. growth factor to enhance stromal cell prodn. of; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Adipose tissue
(adipocyte; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Cartilage
(articular, chondrocytes of, of cows and rabbits; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Acrylic polymers, biological studies
Polyamides, biological studies

Polycarbonates, biological studies
Polyesters, biological studies
Vinyl compounds, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as biocompatible material for three-dimensional framework; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Cotton
(as biodegradable material for three-dimensional framework; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Collagens, biological studies
Gelatins, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as biodegradable material for three-dimensional framework; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Materials
(biocompatible, for three-dimensional framework; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Electron beams
(biodegradable material three-dimensional framework treatment with; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Bone marrow
Placenta
(cells of, from umbilical cord blood; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Umbilical cord
(cells of; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Cattle
Rabbit
(chondrocytes of; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Fluoropolymers, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds., as biocompatible material for three-dimensional framework; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(connective tissue, secreted from stromal cells and enveloping biocompatible three-dimensional framework; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Skin
(dermis, mesenchymal stem cells of; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Blood vessel
(endothelium, cells of; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Carboxylic acids, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters, polyhydroxy, as biodegradable material for three-dimensional framework; three-dimensional cartilage cultures using transforming growth factor-.beta.)

IT Animal cell

(fibroblast-like; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Sponges (artificial)
(framework as mesh or; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Cat (Felis catus)
(gut sutures of, as biodegradable material for three-dimensional framework; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Muscle
(mesenchymal stem cells of; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Growth factors, animal
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nutrient medium contg.; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Culture media
(nutrient; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Transformation, genetic
(of stromal cells with exogenous gene; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Blood
(of umbilical cord, bone marrow cells from; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Capillary vessel
(pericyte; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Lymphocyte
(plasma cell; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Embryo, animal
(stem cell, chondrocyte-progenitor cells; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Mesenchyme
(stem cell; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Adipose tissue
(stromal cell; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Bioreactors
(stromal cells culturing on framework of; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Gene
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(stromal cells transfected with exogenous; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Animal tissue culture
Cartilage
Chondrocyte
Fibroblast
Leukocyte
Macrophage
Mast cell
Monocyte
(three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT Transforming growth factors
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-, nutrient medium contg.; three-dimensional cartilage cultures

using transforming growth factor-.beta.)
IT Transforming growth factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.1-; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT 9002-84-0D, Polytetrafluoroethylene, compds. 9003-07-0 9003-53-6
9004-70-0D, Nitrocellulose, compds.
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as biocompatible material for three-dimensional framework; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT 9004-34-6, Cellulose, biological studies 26009-03-0, Polyglycolic acid
26124-68-5, Polyglycolic acid
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as biodegradable material for three-dimensional framework; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT 75-21-8, Oxirane, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(biodegradable material three-dimensional framework treatment with; three-dimensional cartilage cultures using transforming growth factor-.beta.)
IT 50-81-7, Ascorbic acid, biological studies 299-36-5, Ascorbate, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(culture medium contg.; three-dimensional cartilage cultures using transforming growth factor-.beta.)
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(2) Barnard; Biochem Biophys Acta 1990, V1032, P79 HCAPLUS
(3) Campbell; The Journal of Immunology 1991, V147, P1238 HCAPLUS
(4) Caplan; US 4609551 1986 HCAPLUS
(5) Naughton; US 4721096 1988
(6) Naughton; US 4963489 1990 HCAPLUS
(7) Naughton; US 5032508 1991 HCAPLUS
(8) Naughton; US 5266480 1993 HCAPLUS
(9) Vacanti; US 5041138 1991 HCAPLUS

L78 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:377966 HCAPLUS
DN 126:339296
TI Methods for use of mpl ligands with primitive human stem cells
IN Murray, Lesley J.; Young, Judy C.
PA Sandoz Ltd., Switz.; Systemix, Inc.; Sandoz-Patent-Gmbh; Sandoz-Erfindungen Verwaltungsgesellschaft Mbh
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N005-08
ICS A61K035-28; A61K048-00; C12N015-63
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 3
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 9716535	A2	19970509	WO 1996-EP4698	19961029 <--
	WO 9716535	A3	19970828		
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	US 6060052	A	20000509	US 1995-550167	19951030
	CA 2236263	AA	19970509	CA 1996-2236263	19961029
	AU 9674953	A1	19970522	AU 1996-74953	19961029
	AU 717783	B2	20000330		
	EP 858503	A1	19980819	EP 1996-937284	19961029
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 11514879	T2	19991221	JP 1996-517062	19961029
	US 6326205	B1	20011204	US 1999-328188	19990608
PRAI	US 1995-550167	A	19951030		
	WO 1996-EP4698	W	19961029		

AB Myeloproliferative leukemia receptor (mpl) ligands, such as thrombopoietin, act on a primitive subpopulation of human stem cells having the characteristics of self-renewal and ability to give rise to all hematopoietic cell lineages. Thrombopoietin supports both megakaryocytic differentiation and primitive progenitor cell expansion of CD34+ and CD34 sub-populations (CD34+Lin; CD34+Thy-1+Lin-, and CD34+Lin- Rh12310). Thrombopoietin also stimulates quiescent human stem cells to begin cycling. Thus, mpl ligands are useful for expanding primitive stem cells for restoration of hematopoietic capabilities and for providing modified human stem cells for gene therapy applications.

ST mpl ligand stem cell hematopoiesis; thrombopoietin stem cell hematopoiesis

IT Proteins (specific proteins and subclasses)
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(HIV replication-interfering; mpl ligand and cytokines for providing human stem cells for gene therapy with foreign protein expression)

IT Proteins (specific proteins and subclasses)
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(mdr-related; mpl ligand and cytokines for providing human stem cells for gene therapy with foreign protein expression)

IT Gene therapy
Hematopoiesis
Hematopoietic stem cell
(mpl ligand and cytokines for expanding primitive human stem cells for restoration of hematopoiesis and providing human stem cells for gene therapy)

IT Interleukin 3
Interleukin 6
Leukemia inhibitory factor
Stem cell factor
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mpl ligand and cytokines for expanding primitive human stem cells for restoration of hematopoiesis and providing human stem cells for gene therapy)

IT Antisense DNA
Ribozymes
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(mpl ligand and cytokines for providing human stem cells for gene therapy with foreign gene)

IT Cytokines
Hemoglobins
MDR1 P-glycoprotein
TCR (T-cell receptors)
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(mpl ligand and cytokines for providing human stem cells for gene therapy with foreign protein expression)

IT 9014-42-0, Thrombopoietin 83869-56-1, Granulocyte-macrophage colony-stimulating factor 143011-72-7, Granulocyte colony-stimulating factor
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mpl ligand and cytokines for expanding primitive human stem cells for restoration of hematopoiesis and providing human stem cells for gene therapy)

IT 9001-27-8, Blood-coagulation factor VIII 9001-28-9, Blood-coagulation factor IX 9026-93-1, Adenosine deaminase 37228-64-1, Glucocerebrosidase
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(mpl ligand and cytokines for providing human stem cells for gene therapy with foreign protein expression)

L78 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS
AN 1992:18084 HCAPLUS
DN 116:18084
TI Human hematopoietic stem cells and fluorescence-activated cell sorting in their separation
IN Tsukamoto, Ann; Baum, Charles M.; Aihara, Yukoh; Weissman, Irving
PA Systemix, Inc., USA
SO U.S., 9 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM C12N005-00
ICS C12Q001-00; G01N033-53
NCL 435007210
CC 9-10 (Biochemical Methods)
Section cross-reference(s): 13, 15
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5061620	A	19911029	US 1990-502616	19900330	
	EP 451611	A2	19911016	EP 1991-104813	19910326	<--
	EP 451611	A3	19920122			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
	CA 2039315	AA	19911001	CA 1991-2039315	19910328	
	AU 9173986	A1	19911003	AU 1991-73986	19910328	
	AU 641488	B2	19930923			
	JP 07313150	A2	19951205	JP 1991-133731	19910329	
	JP 3017320	B2	20000306			
	JP 2000078968	A2	20000321	JP 1999-279527	19910329	
	JP 3160600	B2	20010425			
	US 5763197	A	19980609	US 1991-720883	19910625	
	US 5643741	A	19970701	US 1995-466659	19950606	
	US 5716827	A	19980210	US 1995-469452	19950606	
	US 5750397	A	19980512	US 1995-469453	19950606	
	US 5914108	A	19990622	US 1995-466062	19950606	
PRAI	US 1990-502616	A	19900330			
	JP 1991-133731	A3	19910329			
	US 1991-720883	A1	19910625			

AB Human hematopoietic stem cells are provided by sepn. of the stem cells

from dedicated cells using fluorescence-activated cell sorting. Fluorescent-labeled monoclonal antibodies to CD34, CD10, CD19, and CD33 (and Thy-1) antigens are used in the sepn. to obtain CD34+ 10-19-33- (Thy-1+) cells. Methods for assaying for the stem cells as to their capability for producing T-cells, B-cells, and myeloid cells are also described.

ST human hematopoietic stem cell sepn; fluorescence hematopoietic stem cell sorting

IT Lymphocyte
(B-cell, sepd. human hematopoietic stem cells differentiation into, assays for)

IT Antigens
RL: ANST (Analytical study)
(CD19, fluorescent monoclonal antibodies to, for fluorescence-activated cell sorting sepn. of human hematopoietic stem cells)

IT Antigens
RL: ANST (Analytical study)
(CD33, fluorescent monoclonal antibodies to, for fluorescence-activated cell sorting sepn. of human hematopoietic stem cells)

IT Antigens
RL: ANST (Analytical study)
(CD34, fluorescent monoclonal antibodies to, for fluorescence-activated cell sorting sepn. of human hematopoietic stem cells)

IT Lymphocyte
(T-cell, sepd. human hematopoietic stem cells differentiation into, assays for)

IT Antigens
RL: ANST (Analytical study)
(Thy-1, fluorescent monoclonal antibodies to, for fluorescence-activated cell sorting sepn. of human hematopoietic stem cells)

IT Cytometry
(flow, fluorometric, sorting by, of human hematopoietic stem cells, monoclonal antibodies in)

IT Antibodies
RL: ANST (Analytical study)
(monoclonal, conjugates, to CD34 and other antigens, with fluorescent labels, for fluorescence-activated cell sorting sepn. of human hematopoietic stem cells)

IT Hematopoietic precursor cell
(myeloid, sepd. human hematopoietic stem cells differentiation into, assays for)

IT Hematopoietic precursor cell
(stem, human, fluorescence-activated cell sorting sepn. of, monoclonal antibodies in)

IT 82707-54-8, CD10 antigens
RL: ANST (Analytical study)
(fluorescent monoclonal antibodies to, for fluorescence-activated cell sorting sepn. of human hematopoietic stem cells)

IT 50-23-7, Hydrocortisone
RL: ANST (Analytical study)
(human hematopoietic stem cells differentiation into B-cells and myeloid cells in relation to)

=> d his

(FILE 'HOME' ENTERED AT 13:57:23 ON 20 JUN 2002)
SET COST OFF

FILE 'WPIX' ENTERED AT 13:57:34 ON 20 JUN 2002
E KLEIN B/AU
L1 143 S E3-E11
E LU Z/AU

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L2          505 S E3-E7
                E BARTHOLEYNS J/AU
L3           15 S E2,E3
L4            1 S L1 AND L2,L3
L5            1 S L2 AND L3
L6            1 S L4,L5
L7         2946 S MACROPHAG?
L8          129 S L7 AND PROGENITOR?
L9          246 S L7 AND STEM CELL
L10          93 S L7 AND MYELOID
L11           3 S L7 AND MYELO (L) ERYTHRO?
L12          12 S L1-L3 AND L7
L13          31 S L1-L3 AND (MYELOID OR MYELO OR PROGENITOR OR STEM CELL OR CD3
L14          11 S L13 AND L12
L15          11 S L6,L14
L16          21 S L12-L13 NOT L15
L17          10 S L15 NOT FUSION/TI
L18          89 S L7 AND A61K035-14/IC,ICM,ICS
L19          32 S L7 AND A61K035-28/IC,ICM,ICS
L20           7 S L7 AND (B14-F11 OR B12-H06 OR C14-F11 OR C12-H06)/MC
L21         112 S L18-L20
L22          46 S L21 AND (P200 OR P220 OR P433 OR P434)/M0,M1,M2,M3,M4,M5,M6
L23          93 S L7 AND MYELOID
L24          25 S L23 AND PROGENITOR
L25          26 S L23 AND STEM CELL
L26          31 S L23 AND (HEMATOPO? OR HAEMATOPO? OR HEAMATOPO?)
L27          45 S L24-L26
L28          11 S L27 AND (P200 OR P220)/M0,M1,M2,M3,M4,M5,M6
                SEL DN AN 8 9
L29           2 S L28 AND E1-E4
L30          34 S L27 NOT L28
L31           2 S L6,L29
L32           1 S L15 AND L31
L33          10 S L15 NOT L32
L34           2 S L31,L32

     FILE 'WPIX' ENTERED AT 14:30:25 ON 20 JUN 2002

     FILE 'HCAPLUS' ENTERED AT 14:31:25 ON 20 JUN 2002
                E EP1150694/PN
                E WO2000-EP647/AP,PRN
                E EP99-400239/AP,PRN
                E BARTHOLEYNS J/AU
L35          57 S E3-E5
                E KLEIN B/AU
L36         402 S E3-E11,E38
                E LU Z/AU
L37         257 S E3,E20
                E LU ZHAO/AU
L38          36 S E3,E17,E57
L39         730 S L35-L38
L40       85160 S MACROPHAG?
                E MACROPHAGE/CT
                E E3+ALL
L41       42227 S E6,E5
L42       42223 S E5+NT
L43          49 S L39 AND L40,L41,L42
L44       85485 S L40-L42
L45        3003 S L44 AND MYELOID(L)CELL
                E HEMATOPOIETIC PRECURSOR CELL/CT
L46        2021 S E28
L47        3479 S E33
L48         611 S L44 AND L46
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L49          604 S L44 AND L47
L50         2597 S L44 AND STEM(L)CELL
L51         3738 S L44 AND PROGENITOR
L52         3617 S L44 AND PROGENITOR(L)CELL
L53         6870 S L45,L48-L52
L54         1130 S L44 AND CD34
L55         1004 S L53 AND L54
L56         2303 S HEMATOPOIETIC PRECURSOR CELL/CT (L) ERYTHROID
L57          163 S L54 AND L56
L58         1012 S L55,L57
L59         4192 S L44 AND COMPOSITION
L60         1969 S L59 NOT COMPOSITION/CW
L61          139 S L60 AND L53
L62           25 S L60 AND L54
L63           20 S L60 AND L55
L64            7 S L60 AND L57
L65           21 S L60 AND L58
L66          144 S L61-L65
L67          101 S L66 NOT (3 OR 8 OR 7)/SC,SX
L68           14 S 9/SC,SX AND L67
                 SEL DN 7 8 10 11 13
L69            5 S L68 AND E1-E5
L70           93 S L60 AND 9/SC,SX NOT L66
                 SEL DN AN 62
L71            1 S E6-E8 AND L70
L72            6 S L69,L71
L73            6 S L72 AND L35-L72

     FILE 'DPCI' ENTERED AT 14:49:43 ON 20 JUN 2002
                 E EP99-400239/AP,PRN
L74            1 S E4

     FILE 'DPCI' ENTERED AT 14:50:16 ON 20 JUN 2002

     FILE 'HCAPLUS' ENTERED AT 14:50:24 ON 20 JUN 2002
                 E EP241578/PN
L75            1 S E3
                 E EP451611/PN
L76            1 S E3
                 E US5672346/PN
                 E WO0221402/PN
                 E WO09221402/PN
                 E WO9716535/PN
L77            1 S E3
L78            3 S L75-L77

     FILE 'WPIX' ENTERED AT 14:53:50 ON 20 JUN 2002
                 E US5672346/PN
L79            1 S E3
                 E WO9221402/PN
L80            1 S E3
L81            2 S L79,L80

     FILE 'WPIX' ENTERED AT 14:54:16 ON 20 JUN 2002

     FILE 'HCAPLUS' ENTERED AT 14:54:29 ON 20 JUN 2002
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